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STEREOISOMERISM AND THE LAW OF ENTROPY.

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Louguinine[1] determined in 1888 the heat of combustion of maleic, fumaric, citraconic, and mesaconic acids and found the value for maleic and citraconic acids to be greater than that for their stereomers. Stohmann,[2] in the course of his brilliant thermochemical investigations, repeated these experiments, and concluded, after examining the heats of combustion of other stereomeric substances, that the unstable modification has a greater heat of combustion, and further, it loses energy in changing into the stable stereomer.

Klinger[3] first suggested that isomers with identical molecular weight and chemical structure, yet with different amounts of energy, may exist, and he later[4] designated such isomerism as alloergaty. As this chemist believed that we have no sure knowledge in regard to the spatial arrangement of the atoms in stereomers, he classed these substances as examples of alloergaty. Subsequently, Tanatar[5] discussed the subject independ-

[1] Compt. rend., **106**, 1289.
[2] J. prakt. Chem., N. F., **46**, 531.
[3] Ber. d. chem. Ges., **11**, 1026 (1878).
[4] *Ibid.*, **32**, 2194 (1899).
[5] Ann. Chem. (Liebig), **273**, 54 (1893).

ently, and suggested that the spatial arrangement of the atoms and their dynamic condition in stereomeric substances may be correlated, or that a class of isomers may exist, which, although stereomerically identical, contain, notwithstanding, different amounts of energy in their molecules. The latter kind of isomerism Tanatar designated as energy or dynamic isomerism. While it is absolutely certain that a considerable number of isomeric substances cannot be grouped according to the present stereoisomeric classifications,[1] and that some of these substances are remarkably sensitive to the influence of physical and chemical energy, it would seem that little or nothing could be gained at present by the introduction of such views into chemical theory, as these speculations are very vague and their adoption would lead to many unproven, and in some cases improbable, conclusions. On the other hand, the development of any theory of stereoisomerism certainly necessitates the acceptance of Stohmann's rule as a basis in an endeavor to connect the chemical properties and reactions of stereomeric substances with their energy relations. In this way we may succeed in developing a theory based on the fundamental chemical principle known as the law of entropy. At once a very serious obstacle is met with in the meagre thermochemical data which exist on the heat of combustion of stereomeric bodies. It is therefore extremely important for the theory of stereoisomerism that Stohmann[2] has proved that the heats of combustion of isomeric unsaturated acids and their coefficients of conductivity in aqueous solution stand in a direct relationship to one another. *In all cases of stereomeric unsaturated acids, where both these values are known, the same relationship holds true,* and if we make the extremely probable assumption that the proportion of free energy in stereomers, *i. e.*, that part of their whole energy which is freely changeable into other forms, to their bound energy increases directly with the heat of combustion, then not only their properties, but also a considerable number of stereomeric reactions, may be brought into correlation with the law of entropy.

[1] Compare Michael: Ber. d. chem. Ges., **39**, 210.
[2] J. prakt. Chem., N. F., **40**, 358; **46**, 530.

Kekulé,[1] in his memorable paper "Ueber die Constitution und die Metamorphosen der chemischen Verbindungen und über die chemische Natur des Kohlenstoffs," assumed that the first stage in every reaction consists in two molecules attracting each other through their chemical affinity, forming a sort of loosely joined larger molecule, and that in this process the coherence of the atoms decreases, since part of their energy is used up in this mutual attraction by the atoms of the other molecule. Kekulé also assumed that neighboring molecules of the same kind help to decrease the attraction of the atoms of the unlike molecules. In this way he explained mass action as occurring when the molecules that act catalytically are the same as one of the components of the large molecule, and catalysis when they are of a different nature from either of them.

This practically forgotten conception was revived some years ago, and attention was called to its extreme importance in explaining chemical changes.[2] According to the writer, the "Kekulé double molecule" is formed by the attraction of the free energy in two or more unlike molecules, and its formation proceeds with the conversion of more or less of the free energy into bound energy and heat, its stability being determined in this way. Such double molecules are represented by compounds with water of crystallization or by the numerous addition products of saturated organic substances with halhydric acids and halogens.[3] The second stage in chemical action may occur in one of three ways: (*a*) by a double molecule passing over, with further conversion of the free into bound energy, into a much more stable ordinary molecule, a process represented by an addition reaction; (*b*) by a homogeneous; and (*c*) by a heterogeneous double decomposition.[4]

In applying these views to explain the catalytic action of a small amount of hydrochloric acid in converting a large amount

[1] Ann. Chem. (Liebig), **106**, 141.

[2] Michael: Ber. d. chem. Ges., **34**, 4028; **39**, 2139.

[3] See *Ibid.*, **39**, 2570.

[4] Homogeneous is used in the sense that the original substances are reformed, and heterogeneous, that new chemical products are formed in the double decomposition. The first process may occur between a substance and a solvent, and is then the cause of the phenomenon known as electrolytic dissociation. See J. prakt. Chem., N. F., **60**, 429; Ber. d. chem. Ges., **39**, 2570.

of maleic into fumaric acid, we may imagine a system consisting of one molecule of the mineral and a large number of molecules of maleic acid. The first step would be the formation of a double hydrochloric-maleic acid molecule. A more complete addition to form chlorsuccinic acid is impossible for two reasons: firstly, because the surrounding molecules of maleic acid are exerting a strong attractive force on the double molecule in their endeavor to decompose it and to unite in their turn with the liberated hydrochloric acid; and secondly, because the increase of entropy produced by the formation of a single molecule of chlorsuccinic acid would be very slight in comparison with that accompanying the conversion of all the maleic into fumaric acid.[1]

Since the change maleic ⟶ fumaric acid is entropic, we may assume, from a theoretical standpoint, that this reaction is proceeding at ordinary temperature; in order to effect a rapid conversion, we must in some way increase the free energy—which is the deciding factor in the transformation—in maleic acid.

This is what is actually done in the formation of the double molecule, which brings about the concentration of almost all of the free energy in separate molecules of hydrochloric and maleic acids into this double molecule. Now, as the greater free energy of maleic acid over that of fumaric acid shows itself in a greater additive power for hydrochloric acid, it is obvious that the hydrochloric-fumaric acid double molecule could have only a transient existence under these conditions, for it would be decomposed by the maleic acid present. The above processes would be repeated until all the maleic acid is converted into fumaric acid, thus realizing the maximum increase of entropy under the conditions of the experiment.[2]

Some interesting experiments on the conversion of maleic into fumaric acid have been published by Skraup,[3] who found that hydrogen sulphide or sulphur dioxide, alone, do not

[1] It is in agreement with this explanation that if the mineral acid is used in considerable quantity, a mixture of halogen-succinic and fumaric acids is obtained.

[2] This explanation of catalysis is capable of a very general application in organic as well as inorganic reactions.

[3] Monats. Chem., **12**, 107.

change maleic acid in aqueous solution, but when they are used together, a conversion into fumaric acid is partially brought about, that is, the transformation only occurs at the moment of their chemical interaction; he found also that in the action of hydrogen sulphide on certain metallic salts of maleic acid the same conversion is partially effected.[1] Skraup noticed that these reagents are absorbed to a greater extent by an aqueous solution of maleic acid than by the same amount of water, thus indicating the formation of a loose addition product.[2] Assuming this to be the case, and that the double molecule of maleic acid with hydrogen sulphide reacts exothermically with sulphur dioxide or with its double maleic acid molecule, as these substances do in the absence of the acid, we obviously have conditions more favorable for the conversion of maleic into fumaric acid than if the energy were not liberated through the interaction of these double molecules.

The same explanation may be applied to the formation of fumaric acid in the decomposition of metallic maleinates by hydrogen sulphide; the first stage in the reaction is the formation of a double molecule of the salt with hydrogen sulphide, and the energy liberated in its decomposition into metallic sulphide and maleic acid is obviously readily available to facilitate the exothermic change of maleic into fumaric acid. It is also of interest that Skraup found that a very much greater proportion of fumaric acid is formed when the copper, lead, and cadmium salts are decomposed than in the case of the zinc and nickel salts. Judging by analogy from thermochemical data on the decomposition by hydrogen sulphide of other salts of these elements, this is what we should expect, as the heat of formation of the sulphides is greater for the metals of the first than for those of the second group.

A very important factor in determining the extent and facility of the transformation of maleic into fumaric acid lies in the much greater insolubility of the latter acid. The question of

[1] Skraup (*Loc. cit.*, p. 146) assumes two kinds of intramolecular gyration and that certain exothermic reactions may act catalytically by a sort of chemical resonance. Such very indefinite and unlikely conjectures do not contribute to a better understanding of these phenomena.

[2] *Ibid.*, p. 140.

the formation of an insoluble or volatile substance, and its elimination, owing to these properties, from a chemical system which otherwise would be in a condition of reversible equilibrium, may determine the entropy, and in this way the course of a reaction; obviously the same relations must prevail when the equilibrium between two stereomeric bodies is similarly disturbed. Thus, if molten maleic acid (130°) passes over partially into fumaric acid, and at a certain temperature a condition of reversible equilibrium is established, the fact that the latter acid is insoluble in the flux and possesses a higher melting point (258°) would, as long as the flux is kept under that temperature, necessarily lead to a complete conversion into that acid. On the other hand, if we have fumaric acid in a state of flux, the question of insolubility as an entropic factor in determining a chemical change would be eliminated, and that of volatility would arise instead; therefore, in the conversion of fumaric acid into maleic acid at a high temperature and of this into its still more volatile anhydride and water, we have an illustration of the tendency to the formation of volatile as well as endothermic compounds under such conditions.

The stereomeric relations that occur in addition processes are extremely complicated; outside of the group of dibasic, unsaturated acids, they have been best studied with crotonic and cinnamic acids and their derivatives, and some of the reactions in these groups of substances will be considered in connection with the energy relations.

As far as we know, the addition of hydrobromic acid to propylene may proceed with the formation of either propyl bromide or isopropyl bromide, without any structural opposition to its going either way. That it actually occurs in the direction of the maximum increase of entropy, that is, with the formation of isopropyl bromide, agrees with the theory.[1] If we only had the same insight into the differences in the intramolecular arrangement of the atoms in stereomeric bodies as we have into those of structural isomers, and could connect these relationships with the quantity of energy contained in such

[1] Michael: Ber. d. chem. Ges., **39**, 2140; J. prakt. Chem., N. F., **68**, 499.

stereomers as we can with isomeric substances, we should undoubtedly be able to place stereomeric reactions on a much more satisfactory theoretical basis. There will, however, always remain a notable difference between the reactions of structural and of stereomeric substances,[1] as very slight changes in the conditions of the experiment may, in the case of stereomeric compounds, obscure the true nature of the process; the only product which can be isolated may not be the actual primary product but a stereomerized secondary derivative.

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These conditions in stereomeric reactions partially account for the difficulty in developing the subject consistently from a theoretical standpoint. Thus the addition of chlorine to maleic and fumaric acids leads to the formation of stereomeric dichlorides; we also know that it is much more difficult to convert maleic acid dichloride into fumaric acid dichloride than maleic acid into fumaric acid. From this relationship we may conclude that there exists in maleic acid dichloride some entramolecular obstacle to overcome which requires considerable energy, and it thus prevents the free progress of the reaction to the maximum increase of entropy which undoubtidly would be represented by the formation of fumaric acid dichloride. Cinnamic acid corresponds to fumaric acid in its physical properties and stability towards reagents that do not change its chemical composition; nevertheless, chlorine forms with it in the dark[2] or in light free from actinic rays[3] a low melting dichloride; in sunlight, on the contrary, only a higher melting stereomer is formed. Since these addition products stand in the same relation to each other that maleic acid dichloride does to fumaric acid dichloride, we are forced to the conclusion that cinnamic acid and chlorine give a maleinoid addition product as the primary result. How can we explain this remarkable effect of sunlight in effecting, even if the experiment is made in the cold, so complete a conversion of the lower into the higher melting dichloride that the first product escaped detection until the addition was made in the dark? There are two explanations:

[1] This statement is made with the reservation that desmotropic structural isomerism is excluded.

[2] Liebermann and Finkenbeiner: Ber. d. chem. Ges., **28**, 2226.

[3] See the following paper.

We may suppose that the double molecule of cinnamic acid and chlorine, unassisted by actinic energy, can form only the ordinary cinnamic acid allodichloride molecule; but at the moment of the change of double into single molecule and with the help of actinic rays, it then possesses sufficient chemical momentum to realize, in the formation of the higher melting dichloride, the maximum condition of entropy; or, what seems a less probable explanation, it may be that only in actinic light can the allodichloride unite with chlorine to form a double molecule, and that this possesses the free energy necessary to cause the entropic change[4] into cinnamic acid dichloride and chlorine. An experimental confirmation of either of these interpretations is by no means impossible; at present, however, much greater importance is to be attached to the fact that the primary as well as the final product in stereomeric addition reactions is dependent on the chemical nature of these bodies, and also on that of the additive substance—in other words, on the entropy of the reaction[1]—and that this relationship effectively debars all mechanical explanations of these changes.[2]

The differences between the stereomeric results obtained by additions to fumaric, maleic, and cinnamic acids also appear in the corresponding acetylene acids, but since stereoisomerism in the latter series does not exist, the possibility of a stereoisomerization by the additive reagent before the addition process occurs is here excluded. Acetylenedicarboxylic acid and hydrobromic acid give the higher melting, chemically more stable and more entropic of the two stereomers, that is, bromfumaric acid, as direct product of the reaction; with phenylpropiolic acid a mixture of two β-bromcinnamic acids[3] is obtained, consisting largely of the product melting at 157°, which, although it has a higher melting point than the other β-brom acid (134°), gives allocinnamic acid on reduction.[4] To what extent this result depends on the nature of the additive reagent is seen when acetylenedicarboxylic and phenylpropiolic acids are reduced in

[1] Michael: Ber. d. chem. Ges., **34**, 3646.
[2] J. prakt. Chem., N. F., **75**, 117.
[3] Michael and Browne: Ber. d. chem. Ges., **19**, 1378; **20**, 550.
[4] Liebermann and Scholz: *Ibid.*, **28**, 951.

aqueous solution with zinc, for here the results are comparable, fumaric and cinnamic acids being formed. These last additions proceed, therefore, according to the relations of maximum entropy, for we know that these acids contain considerably less energy than their alloisomers.

Unfortunately, we are not at present in possession of any data which enable us to connect the peculiar behavior shown by phenylpropiolic and cinnamic acids towards hydrobromic acid and chlorine with the energy relations developed in the addition products formed. We do know, however, that energy supplied by halhydric acids, or in the form of heat, may give the chemical momentum necessary to realize the transformation of a maleinoid into a fumaroid acid, when the first-named product shows the greater acidity; also, that the more acidic of these stereomers shows the greater solubility in water. It is of interest, therefore, to trace the connection between the halogen derivatives of the crotonic and cinnamic acids and these relations. The α-monohalogen derivatives of the stereomeric crotonic and cinnamic acids[1] exhibit a behavior analogous to that of the unsubstituted acids; the lower melting stereomer possesses a decidedly greater acidity constant,[2] is more soluble, and when heated or treated with halhydric acids passes over into the higher melting fumaroid derivative. Of the two β-chlorcrotonic acids, the higher melting product (94°) is formed on the addition of hydrochloric acid to tetrolic acid,[3] and gives crotonic acid on reduction. Notwithstanding these properties, it has a larger acidity constant[4] than β-chlorisocrotonic acid, (59°) and therefore should contain a greater amount of free

[1] Michael: J. prakt. Chem., N. F., **52**, 345.

[2] The value for α-bromcinnamic acid (130°) is quoted as 1.44, and that of its stereomer (120°) as 0.093, obviously an inverse relationship to that stated above. This contradiction is due to a curious mistake made by Ostwald (Z. physik. Chem., **3**, 278). In his first paper (J. prakt. Chem., **32**, 367) the classification of Barisch (*Ibid.*, **30**, 185) is accepted as correct: that is, the acid melting at 130° is considered as a β, and that melting at 120° as an α derivative. In this paper, Ostwald shows that the latter acid is considerably more acidic and explains this fact by a greater proximity of halogen to carboxyl. In his subsequent paper, he uses the Glaser classification (Ann. Chem. (Liebig), **143**, 330), which is the opposite to that of Barisch, although the experimental results are still given according to the views of Barisch.

[3] Friedrich: Ann. Chem. (Liebig), **219**, 370.

[4] Ostwald (Z. physik. Chem., **3**, 245). This investigator emphasizes the apparent discrepancy in the acidity constants of these acids.

energy. In accordance with this relationship of their respective energies, the higher melting, apparently fumaroid β-chlorcrotonic acid is convertible by heat into the lower melting β-chlorisocrotonic acid, and is also the more soluble[1] of the two stereomers.

The addition of hydrobromic acid to phenylpropiolic acid gives principally the β-bromallocinnamic acid melting at 159°, which is reducible to allocinnamic acid,[2] and is also convertible by heat into the lower melting (134°) stereomer.[3] These relations agree with those in the crotonic series in the sense that, contrary to those holding for the mother substances and their α-halogen derivatives, the higher melting β-halogen acid goes over on heating into the lower melting stereomer; unfortunately, the acidity values in the cinnamic series have not been determined, so that the connection between these factors and stability towards heat cannot be traced.

It has already been stated that the reactions of stereomeric isomers are distinguishable from those of structural isomers in that the former are much more sensitive than the latter to any physical or chemical influence that may change the entropy of the reaction. This relation must be constantly kept in mind in stereochemical investigations; indeed, there is no exaggeration in the statement that the present confused condition of the theory is, in no small measure, due to the purely mechanical conceptions by which stereomeric processes are judged.[4] For illustration, two cases will be considered: Cinnamic acid dibromide (201°), when decomposed by alcoholic potash, yields a mixture of α-bromcinnamic and α-bromallocinnamic acids, in the proportion of about one part to seven; but if the ethyl ester corresponding to this dibrom acid is treated in the same manner the above relation in

[1] Kahlbaum: Ber. d. chem. Ges., **12**, 2339.

[2] Hydrochloric acid and phenylpropiolic acid unite to form two β-chlorcinnamic acids (Michael and Pendleton: J. prakt. Chem. **40**, 65), but their behavior on reduction has not been examined. How sensitive such reactions may be is shown by the fact that hydriodic acid also forms two β-iodocinnamic acids, but they are both reducible to cinnamic acid (Michael and Whitehorne: Ber. d. chem. Ges., **34**, 3660).

[3] Erlenmeyer: Ann. Chem. (Liebig), **253**, 23.

[4] Since optical isomerism is not strictly speaking a chemical phenomenon, but a mechanical result, it has been possible to correlate facts and theory very successfully by means of the mechanical Le Bel-van't Hoff theory. See Ber. d. chem. Ges., **34**, 3647; J. prakt. Chem., N. F., **75**, 117.

the quantities of the α-bromcinnamic acids is reversed, being changed to about ten parts to seven.[1] The primary action of potash on cinnamic acid dibromide is to form the corresponding salt; this is followed by the elimination of hydrobromic acid to form α-bromcinnamate. If we assume that there is only a slight intramolecular obstacle to the development of the maximum entropy in the elimination process, it should proceed largely with the formation of the salt of α-bromallocinnamic acid, as this acid is more acidic than its stereomer and should be better neutralized by the strongly positive potassium.[2] Sudborough and Thompson[3] have shown that the primary action of alcoholic potash on the ester dibromide is the abstraction of hydrobromic acid before saponification occurs. Starting, therefore, with the ethyl ester instead of the acid, and assuming, as with the potassium salt, that there is no especial hindrance to the development of maximum entropy in the elimination process, we have this problem: which of the two α-bromcinnamic acids will better neutralize an ethyl radical? In the fact that ethyl requires for neutralization a less acidic acid than potassium, we have the explanation why the ester of the less acidic α-bromcinnamic acid is formed in greater proportion to that of α-allobromcinnamic acid[4] than in the above case of the potassium derivatives.

Before considering the stereomeric relations between maleic and fumaric acids and their addition products, I wish to discuss

[1] Sudborough and Thompson: J. Chem. Soc., **83**, 676 (1903). These chemists have overlooked the fact that this reversal in the relative amounts of the α-brom acids, when the ester is used, was first noticed by me in 1887 (THIS JOURNAL, **9**, 280). At the same time, it was proved that the same relation appears when α,β-dibrom- and α,β-dichlorbutyric acids and their ethyl esters are treated with alkalis.

[2] An application of the law of chemical neutralization; see Ber. d. chem. Ges., **38**, 23.

[3] J. Chem. Soc., **83**, 678.

[4] This relationship explains why phenylpropiolic acid may be obtained purer and more readily from the ester than from free cinnamic acid dibromide, since α-bromcinnamic acid loses hydrobromic acid more easily than the α-allo acid. If a mixture of these two acids is available for the preparation of phenylpropiolic acid, it is obviously advantageous to convert the latter into the former acid by heating, as Whitehorne and myself (Ber. d. chem. Ges., **34**, 3648) have already recommended. Our method consisted in melting the mixture in a platinum crucible and then, *without removing the flame*, keeping it in a molten condition for about a minute. Unfortunately, we did not state explicitly that the flame was not removed, and Sudborough and Thompson (J. Chem. Soc., **83**, 686) have therefore assumed that the mixture was heated no higher than its melting point; they prove that the amount converted is slight at that temperature.

briefly a recent attempt of Pfeiffer[1] to modify the van't Hoff hypothesis in such a manner as to reconcile facts and theory. When it was proved[2] that the higher melting fumaroid modification of the stereomeric halogen-succinic acids loses halhydric acid or halogen more readily than the lower melting maleinoid stereomer, and that fumaric derivatives are direct products of the addition of these reagents to acetylenedicarboxylic acid, attention[3] was directed to the fact that Wislicenus and other chemists had based various configurations on the false assumption that additions always proceed with formation of *cis* products, and that eliminations take place more easily with these than with the trans stereomers.

It was also stated that if chemists still deemed it desirable to employ configurations, it would be necessary to accept the power to form anhydrides as the test in classifying the unsaturated dibasic acids, and the configurations hitherto assigned to all other stereomers would have to be reversed. The above results have led to the classing of additions and eliminations as *trans* as well as *cis* processes; but, accepting the van't Hoff configuration for acetylenedicarboxylic acid and basing those of the stereomeric dibasic unsaturated acids on the property of anhydride formation, these terms convey a false impression, since such *trans* reactions can take place only when accompanied by intramolecular rearrangements. Pfeiffer assumes that all additions and eliminations with halogen and halhydric acid are *trans*, and that the carboxyl groups in acetylenedicarboxylic acid are in a *trans* position to each other. This fundamental assumption, that additions and eliminations are *trans* processes, was considered by the writer[4] in 1889, when attention was called to the fact that in this way certain reactions which stand in contradiction to Wislicenus's views, and *vice versa*, could be explained. In connecting facts with theory Pfeiffer's ideas are far inferior to those of van't Hoff. Thus, according to van't Hoff's views, the existence of but one acetylenedicarboxylic acid is explained, while, according to Pfeiffer's

[1] Z. physik. Chem., **48**, 40 (1904).
[2] Michael: J. prakt. Chem., N. F., **52**, 291 (1895).
[3] *Ibid.*, **52**, 290 (1895).
[4] *Ibid.*, **38**, 349.

hypothesis, there is no reason why a maleinoid as well as a fumaroid modification of this acid should not exist, and the remarkable acidity[1] of the acid is hardly compatible with the assumption that the mutual relations of the carboxyl groups in it are comparable to those in the relatively weak fumaric (K: 0.093) and not to those in maleic acid (K: 1.17). Indeed, Pfeiffer appears to have overlooked the important relationship between acidity and the configurations of stereomeric acids. Thus, although he accepts the van't Hoff configurations for maleic and fumaric acids, which explain the greater acidity of maleic acid, yet in his configurations for the crotonic acids and their α-chlor derivatives, methyl and carboxyl are in the *cis* position for the stronger acid. The contradiction between his assumption for monobasic and dibasic acids is obvious.

Moreover, Pfeiffer has not considered the fact that the ease of elimination in a *trans* or *cis* position is only a proportionate relation, and that with some substances it takes place quite readily when, in his own configurations, the eliminated parts are in the *cis* position. Indeed, with saturated stereomers there seems to be little or no difference between them in this respect.[2] Further, in many reactions it has been conclusively proved that there is formed simultaneously in the addition process a mixture of stereomers whose relative proportions depend on conditions absolutely incompatible with any mechanical conceptions of the processes.[3]

It is known that maleic acid contains more energy and has a greater acidity constant than fumaric acid; also, in respect to the latter factor, that racemic has a greater value than meso-tartaric acid. Fortunately, the constants K for the acid sodium salts of maleic and fumaric acids have been ascertained, with the result that although fumaric has a much smaller constant than maleic acid, in the case of the acid salts this relation is reversed, the fumarate having a greater value than

[1] Acetylenedicarboxylic acid is almost as strong as sulphuric acid (Ostwald: Z. physik. Chem., **3**, 380).

[2] Michael and Mighill: Ber. d. chem. Ges., **34**, 4221.

[3] Straus (Ann. Chem. (Liebig), **342**, 211) has mentioned a number of specific cases showing the inadequacy of Pfeiffer's views. Their number could easily be enlarged, but it seems hardly necessary.

the maleinate.[1] From these results it would appear that in the formation of these acid salts the energy relations existing in the acids undergo a reversal, and as it is unlikely that the formation of the neutral from the acid salts is accompanied by another reversal, these data indicate that sodium fumarate contains more energy than sodium maleinate. Starting from this point of view, we should expect that the addition of hydroxyl to sodium fumarate would give the sodium salt of that modification of tartaric acid which has the greater acidity constant, and that from the maleinate we should obtain the salt of the form possessing the lower constant. This is indeed the case, as Kekulé and Anschütz[2] obtained the salt of racemic acid (K : 0.097) from the fumarate and that of mesotartaric acid (K : 0.060) from the maleinate.

Perkin and Duppa,[3] and also Kekulé,[4] obtained, by heating the silver salt of dibromsuccinic acid with water, a tartaric acid which according to Pasteur[5] was racemic acid, but which Jungfleisch[6] showed subsequently to consist of a mixture of racemic and mesotartaric acids. Later, Demuth and Meyer[7] made an analogous experiment with silver isodibromsuccinate, obtaining in this way racemic acid almost quantitatively. The conversion of the stereomeric dibrom- into dihydroxysuccinic acids by boiling with water has been minutely studied by Lossen and Riebensahm,[8] who found that a mixture of racemic and mesotartaric acids is formed in each case, but that dibromsuccinic acid gives principally mesotartaric acid and the isodibrom acid mainly racemic acid. From these results, it appears that fumaric and mesotartaric acids, and maleic and racemic acids, are very closely connected chemically. Werner[9] explains the evident contradiction between this conclusion and that based on the results obtained by direct oxi-

[1] Trevor: Z. physik. Chem., **10**, 350; Smith: *Ibid.*, **25**, 242. See also Ostwald: *Ibid.* **9**, 558.

[2] Ber. d. chem. Ges., **13**, 2150; **14**, 713.

[3] J. Chem. Soc., **13**, 102.

[4] Ann. Chem. (Liebig), **117**, 120.

[5] Ann. Chim. Phys., [3], **61**, 484.

[6] Bull. Soc. Chim., [2], **19**, 194.

[7] Ber. d. chem. Ges., **21**, 268.

[8] Ann. Chem. (Liebig), **292**, 295; also, Lossen and Reisch: *Ibid.*, **300**, 5.

[9] Lehrb. d. Stereochemie, p. 226; also p. 204.

dation of the salts by assuming that when bromine is added to maleic and fumaric acids a *trans* addition takes place; with hydroxyl, on the contrary, the addition is *cis*.[1] There is, however, no reason why the proportionate relations in the acidity constants for maleic and fumaric acids should undergo a relative change in their conversion, first, into their dibrom addition products, and afterwards, through the action of water, into dihydroxysuccinic acids. Since racemic has a greater acidity constant than mesotartaric acid, the fact that maleic acid, through its dibromide, gives racemic acid agrees with the energy relations. An interesting confirmation that this is the true relationship may be found in an investigation by Walden[2] on the influence that stereomeric acids have on the rotatory power of their *l*-amyl esters. He found that the fumaric and mesaconic esters show a greater molecular rotatory power than the maleic and citraconic esters; also, that this is true for mesotartaric as compared with racemic amyl ester. These results obviously connect maleic and racemic esters; but, under the impression that fumaric and racemic esters are chemically related, Walden[3] calls attention to the discrepancy which he supposes exists between the stereomeric conclusions derived from the investigations of these acids by a chemical and by a physical method.

Twenty years of ardent stereochemical investigation has led to a considerable increase in the number of compounds that, sometimes rightly and sometimes wrongly,[4] have been classified as belonging to the category of stereomers, and a number of empirical laws in regard to the relations between the physical and chemical properties of such substances have been formulated.

Fortunately in recent years there has been a slow awakening; the belief that the intramolecular relations of the atoms in stereomers can be ascertained by mechanical speculations, and that the intricate chemical relations of such bodies

[1] Since *trans* additions must in these cases be accompanied by a shifting in the position occupied by carboxyl or hydrogen, and as there is no apparent reason for such complicated changes, such assumptions are of very doubtful value.

[2] Z. physik. Chem., **20**, 377.

[3] *Ibid.*, **20**, 386.

[4] See Ber. d. chem. Ges., **39**, 209.

can ever be correlated to a mechanical system is being gradually abandoned.[1]

One of the chief objects of this paper is to call attention to the intimate connection between the energy relations of stereomeric substances and their chemical behavior; further, to point out that our surest sources of information on this subject have been systematically neglected, and to urge the absolute necessity, therefore, of such thermochemical and physicochemical investigations of stereomeric bodies as may lead to the development of a consistent theoretical treatment of the subject.

TUFTS COLLEGE, MASS.

THE ADDITION OF HALOGENS TO CINNAMIC ACID AND SOME OF ITS DERIVATIVES.[2]

BY ARTHUR MICHAEL AND HOWARD D. SMITH.

In an experimental investigation, designed to test the validity of the assumptions on which J. Wislicenus had based his methods for determining the configurations of stereomeric substances, it was shown by one of us[3] that the application of his views to unsaturated, stereomeric dibasic acids led to configurations diametrically opposed to those derived from a consideration of the property of forming anhydrides. Thus, if we base the *cis* relationship of the carboxyl groups on the ability of such an acid to form an anhydride, we must classify bromfumaric acid as a *trans* derivative; on the other hand, if we start from the equally valid argument that with a *cis* relationship existing between the hydrogen and bromine a more ready elimination of bromhydric acid takes place than when these elements are in a *trans* position, we must denote the same acid by a *cis* configuration. If we accept the assumption in regard to anhydride formation as correct, we are forced to the conclusion that additions and eliminations do not take place as *cis*, but mainly as *trans* processes; and, starting from this idea

[1] See J. prakt. Chem., N. F., **75**, 117.

[2] This research is not completed, but as Herz and Mylius (Ber. d. chem Ges., **39**, 3816) and Sudborough and Thomas (P. Chem. Soc., **22**, 318) have recently published work bearing on the same subject, it was thought advisable to publish our results.

[3] Michael: J. prakt. Chem., N. F., **52**, 289.

as a means of classifying stereomeric unsaturated compounds, all configurations which Wislicenus and his supporters had previously assigned to unsaturated substances have to be reversed,[1] excepting, of course, those of the unsaturated dibasic acids which are based on the property of forming anhydrides. While this fundamental contradiction between the methods for determining configurations obviously made all speculations on the intramolecular arrangement of atoms in stereomers of very doubtful value, yet the application of the addition-elimination principle[2] to the classification of stereomeric substances provided at least a means of expressing in general laws the relationship between the physical and chemical properties of such stereomers.[3] Thus, of two unsaturated stereomeric acids, that denoted by the unstable maleinoid condition should melt at a lower temperature and be more soluble than the other form. The same relationship appears also in the halogen derivatives of these acids. The higher melting of these stereomers is the one which is formed by the addition of halhydric acid or halogen from the corresponding acetylenecarboxylic acid, and it, in turn, also gives up the addenda more easily than the lower melting, maleinoid acid in re-forming the mother substance.

Until 1895, these generalizations were also applicable to the stereomeric cinnamic acids and their derivatives, but in that year, Liebermann and Finkenbeiner[4] made the important observation that when chlorine is added to cinnamic acid in the dark a cinnamic acid dichloride melting at 86°, instead of the stereomeric product melting at 168°,[5] is formed. Judging

[1] Michael: J. prakt. Chem., N. F., **52**, 359.

[2] Werner (Lehr. der Stereochemie, p. 210) remarks that the law governing the relations between the formation of stereomeric addition products and their reconversion into the original substances (Michael: Ber. d. chem. Ges., **34**, 4215) may be considered probable, as it harmonizes with the conception that the formation of stable proceeds through those of unstable modifications. The comparison is untenable, for in structural addition reactions the actual product is always the more stable of the possible isomers, *under the conditions of its formation*, and the same relationship exists in stereomeric additions. Werner has overlooked the fact that the experimental conditions in the elimination are entirely different from those in the addition experiments. (A. M.)

[3] J. prakt. Chem., **52**, 344.

[4] Ber. d. chem. Ges., **28**, 2235.

[5] Erlenmeyer: *Ibid.*, **14**, 1867.

from this result, it would seem as if the higher melting dichloride were not the primary addition product of cinnamic, but of allocinnamic, acid. This view is apparently confirmed by the fact that with the same conditions under which cinnamic acid gives the lower melting dichloride quantitatively, allocinnamic acid yields mainly the higher melting stereomer.[1]

In apparent contradiction to this view are the observations that both allocinnamic acid and its methyl ester, treated in the dark with an excess of bromine, give 30–40 per cent of a lower melting dibromide along with the ordinary form, and that these lower melting products are not obtained from cinnamic acid and its ester under the same experimental conditions.[2]

An interesting contribution to this subject was made by Plöchl and Mayer,[3] who showed that the phenylglyceric acid (141°) formed by the mild oxidation of cinnamic acid[4] could not be resolved into optically active components; further, a stereomer (120°) obtained from the higher melting cinnamic dibromide[5] was shown in this way to possess a racemic structure. A comparison of these results with those obtained in similar experiments with maleic and fumaric acids[6] led these chemists to the conclusion that cinnamic acid is not chemically related to fumaric, but to maleic, acid. Several years later,[7] it was shown that by using carbon tetrachloride as a solvent and adding the bromine to cinnamic ethyl ester in the dark, over 50 per cent, and from methyl cinnamate about 35 per cent, of allodibromides, along with the higher melting dibromides, could be obtained. Furthermore, the methyl ester allodibromide formed in this way is identical with the product which Liebermann[8] had previously obtained (mixed with 50–60 per cent of the stereomer) from methyl allocinnamate, thus proving definitely that the addition of bromine to cinnamic

[1] Liebermann: Ber. d. chem. Ges., **27**, 2040.
[2] *Ibid.*, **24**, 1108; **27**, 2038.
[3] *Ibid.*, **30**, 1600.
[4] Fittig and Ruer: Ann. Chem. (Liebig), **268**, 27.
[5] Anschütz and Kinnicutt: Ber. d. chem. Ges., **12**, 537.
[6] Kekulé and Anschütz: *Ibid.*, **14**, 713.
[7] Michael and Whitehorne: *Ibid.*, **24**, 3660.
[8] Ber. d. chem. Ges., **24**, 1107.

and allocinnamic derivatives, under certain conditions, may give the same allodibromide. Allocinnamic acid was also oxidized with potassium permanganate and the lower melting racemic phenylglyceric acid (120°) obtained in this way.

The experiments on the formation of ethyl cinnamate allodibromide from ethyl cinnamate and bromine were repeated by Sudborough and Thompson,[1] but for some unknown reason these chemists were unable to observe the formation of more than a trace of the allodibromide. This led us to repeat the experiments of Michael and Whitehorne, and our results are practically identical with theirs. It was emphasized in the former paper[2] that the proportion of allodibromide to dibromide formed in these reactions is dependent on very subtle conditions; although we have made a number of new experiments to enable us to define these more precisely than before, we have not succeeded in accomplishing our object. It may be stated, however, that in thirty experiments, using carbon tetrachloride as a solvent and adding the bromine in the dark, we always obtained some allodibromide, no matter in what other respect the conditions of the experiment were changed; indeed, in some of the experiments almost 50 per cent of the mixture consisted of this product.

Liebermann and Finkenbeiner[3] prepared cinnamic acid allodichloride by passing an excess of chlorine into a mixture of cinnamic acid and carbon tetrachloride, the necessary precautions for a successful result being (*a*) that the mixture should be carefully cooled with ice, (*b*) kept in the dark during the operation, and (*c*) then allowed to stand without shaking 8–14 days in an ice chest. The solution obtained in this way, after evaporation of the solvent in a vacuum desiccator and subsequent standing for 3–4 days in a cool, dark place, yielded the allodichloride as an oil. This product could be obtained in crystalline form only by a tedious process of purification through the cinchonidine salt, although the oil could be made to solidify by the addition of a small amount of the crystalline acid. Judging from the results of our experiments, it does not seem

[1] J. Chem. Soc., **83**, 671 (1903).
[2] Ber. d. chem. Ges., **34**, 3662.
[3] *Ibid.*, **28**, 2236.

at all necessary to follow these laborious directions. We find that when a cold mixture of cinnamic acid and a solution of chlorine in carbon tetrachloride is exposed to strong, direct sunlight, mainly the higher melting dichloride is formed, although a relatively small amount of the stereomer is also obtained. The proportion of the latter to the former acid is very considerably increased, however, if rays of sunlight are first passed through solutions capable of absorbing the violet end of the spectrum. This result indicates that the conversion of the allodichloride into the ordinary dichloride may be attributed to absorption of energy from the actinic light rays.[1] Furthermore, this conversion is largely dependent on the intensity of the white light, for we noticed that the addition proceeds with the formation of a considerable quantity of allodichloride if the operation is carried out in diffused light. According to our observations all the other precautions so scrupulously observed by Liebermann and Finkenbeiner are immaterial and may be disregarded.

By using the methyl ester instead of cinnamic acid very similar results were obtained: in sunlight, practically only the high melting ester dichloride (101°) is formed; in diffused light, a mixture of this substance with the oily allodichloride; and in the dark, practically nothing except the latter substance.[2] Cinnamyl chloride gave analogous results: in the dark, an oily dichloride, corresponding to cinnamic acid allodichloride; in bright sunlight, a solid addition product which yielded cinnamic acid dichloride when decomposed by water.

Cinnamic acid, although in its physical properties, energy relations, and stability towards all chemical reagents that do not change its chemical nature, so distinctively a fumaroid derivative, yields, notwithstanding, with chlorine the unstable allodichloride as the primary addition product. The maleinoid allocinnamic acid, on the other hand, gives the more stable higher melting dichloride, although the comparatively small amount of oily dichloride formed along with the high melting body may, indeed, prove to be the lower melting

[1] See explanation in the preceding paper.

[2] Compare Liebermann: Ber. d. chem. Ges., **28**, 2239.

dichloride.[1] Such a result is best explained, however, on the assumption that the latter is formed indirectly from some cinnamic acid previously stereomerized by the action of the halogen on the allocinnamic acid. The results obtained by the addition of bromine to the stereomeric cinnamic acids are also, as yet, best explained when considered from the same point of view.

In the cinnamic series, the conditions governing addition reactions vary with the nature of the additive reagent to an extent quite unknown in other groups of unsaturated acids. Under conditions where the allodichloride is formed quantitatively from cinnamic acid, allodibromide is obtained in a comparatively small amount,[2] and in the action of bromine on cinnamic ester the yield of allodibromide depends to a considerable extent on the solvent used.

In the preceding paper, one of us has endeavored to show that a reversal in the energy relations between maleic and fumaric acids takes place when these acids are converted into salts; under such conditions maleic acid is related to racemic and not to mesotartaric acid. As far as we can judge at present, such a reversal does not occur when the stereomeric monobasic cinnamic acids are converted into salts; this view is confirmed by the facts that mesophenylglyceric acid is formed in the oxidation of potassium cinnamate, and that the higher melting cinnamic acid dibromide, which is not the primary but the secondary product of the addition, has been converted into racemic phenylglyceric acid. Sudborough and Thompson[3] have advanced, as an argument against the conclusion that the high melting ethyl cinnamate dibromide (76°) is not the primary addition product of cinnamic, but of allocinnamic, ester, the fact that in this case the high melting cinnamic acid dibromide should give α-bromcinnamic acid on

[1] Several experiments were made on the addition of chlorine to allocinnamic acid and under different conditions we succeeded in obtaining a greater proportion of an oily dichloride than Liebermann. It seems doubtful if the product is identical with that obtained from cinnamic acid, as it is less soluble in petroleum ether. These experiments will be continued.

[2] I intend to make further experiments on the addition of bromine to cinnamic acid, with special reference to the conditions that Liebermann employed when he succeeded in obtaining some allodibromide from allocinnamic acid. (A.M.)

[3] J. Chem. Soc., **83**, 678.

treatment with alkalis, whereas mainly α-bromallocinnamic acid is formed. This behavior cannot be considered a valid objection, since it is based on analogy and on views which seek to explain such chemical processes from a mechanical standpoint. A similar argument would make the primary formation of the unstable allodichloride from the stable cinnamic acid an impossibility, because the addition of chlorine to fumaric acid yields a fumaroid product. Indeed, in the same paper,[1] Sudborough and Thompson show how little value is to be placed on such speculations about stereomeric relations, since they prove that by decomposing the ethyl ester instead of the acid, the relative proportions are reversed, the reaction proceeding with the formation of considerably more α-bromcinnamic than of α-bromallocinnamic acid.[2]

Addition of Chlorine to Cinnamic Acid.

Instead of suspending cinnamic acid in carbon tetrachloride and then passing into the mixture rather more than the theoretical amount of chlorine,[3] the finely pulverized acid was added to a solution of chlorine in the same solvent.[4] The latter was saturated at ordinary temperature, and was of known strength, containing somewhat more halogen than required by the theory.

I. Five grams of cinnamic acid were added to the chlorine solution, contained in a brown glass bottle. This was packed in a tin can, which was then covered and placed in an ice chest. After standing one day, the contents of the bottle were examined in yellow light and found still to contain a considerable amount of undissolved cinnamic acid, which, however, in the course of another day, had almost all disappeared. After standing four days a clear solution had formed, which contained some free chlorine and a little hydrochloric acid; moreover, a very small amount of the crystalline higher melting dichloride had separated out. After distilling off the solvent and exhausting in a vacuum to constant weight, a thick oily residue, 7.1

[1] p. 676.
[2] Explained in the preceding paper.
[3] Liebermann and Finkenbeiner: Ber. d. chem. Ges., **28**, 2236.
[4] Michael: J. prakt. Chem., N. F., **46**, 225.

grams (theory 7.49), of the addition product was obtained. Part of the oil was then dissolved in petroleum ether (60°–70°), and as the allodichloride did not separate out, almost all the solvent was driven off by heating the solution, and the residue placed in the ice chest. After standing three days it had partially solidified, yet even after a month there still remained a small amount of oil mixed with the crystals. The oil which had not been treated with petroleum ether also partially solidified on standing, but this took place more slowly. The product, after being dried on a porous plate, melted at 80–84° and was almost pure allodichloride (84°–86°).

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II. The experiment was repeated, using a brown glass bottle, which excluded the violet rays, and placing it in an ordinary glass beaker containing ice water, in direct sunlight. The addition proceeded more slowly than when the mixture was in a colorless glass bottle; after three hours' exposure to sunlight there still remained considerable unchanged cinnamic acid. During the night the addition was completed, and a small quantity of the high melting dichloride separated out. The oily residue, after removal of the solvent, gradually crystallized, but the product apparently contained some of the higher melting dichloride, as it melted from 75°–100°.

III. Number II. was repeated, except that the brown glass bottle was placed in the focus of a mirror, and exposed to strong sunlight during two days. The addition took place much more rapidly, and some of the high melting dichloride had formed after exposure for several hours. At the end of the experiment more than two-thirds of the addition product consisted of the high melting dichloride.

IV. Like II., but the mixture was placed in a white glass bottle and the day was cloudy. On exposure to light the mixture heated perceptibly, and it was then cooled in ice water. After two hours all the halogen had disappeared. The precipitate (5.9 grams) consisted of dichloride, and the filtrate yielded 0.9 gram oil. The oil was a mixture of dichloride and allodichloride.

V. Repeated IV. on a very cloudy day, cooling off at once in ice water. The chlorine had disappeared after 3–4 hours'

exposure. Obtained 3.8 grams of dichloride and 3.2 grams of allodichloride from the solvent.

VI. Repeated IV., using an ordinary bottle, and leaving the mixture without external cooling in the dark part of a room and out of the direct line of light from a window. After standing for a day all the cinnamic acid went into solution, and in the course of another day a very small amount of dichloride separated out. The solution gave almost the theoretical quantity of an oil, about three-fourths of which gradually solidified. It consisted of allodichloride. This experiment was repeated several times with the same result.

VII. Repeated VI., placing the bottle in diffused light, but in the rear part of the room. During the day it was exposed for several hours to direct sunlight. We obtained 2.5 grams of chloride and 5.6 grams of allodichloride.

VIII. Two grams of cinnamic acid and a slight excess of chlorine in tetrachloride solution were brought, in yellow light, into a colorless glass bottle, which was then placed in a box that admitted only light passing through a prism. This prism contained a 2 per cent solution of potassium bichromate, and cut off all rays of light excepting red, yellow, orange, and green. The box was so placed in bright sunlight that the contents of the bottle were exposed to the light passing through the prism. The addition took place very much more slowly than in white light. This experiment gave 1.7 grams dichloride and 1.05 grams allodichloride, and on repetition 1.8 grams of the former and 1.0 grams of the latter product. At the same time, an experiment was made in which the mixture was exposed to ordinary sunlight; only the dichloride was obtained as a result.

IX. The preceding experiment was repeated, using a 1 per cent solution of iodine in alcohol in the prism. The addition took place very much more slowly than in white light, and a mixture of the stereomeric dichlorides was obtained.

The oily addition product formed in the above experiments contained a small amount of the higher melting dichloride. The greater part of this product was removed by extracting the mixture with a very small amount of benzene and, after allowing it to stand for a day in the ice chest, filtering off the dichloride that separated out. The oil remaining after evapo-

ration of the solvent gradually crystallized, and on drying on a porous plate was found to be almost pure allodichloride.

Addition of Chlorine to Methyl Cinnamate.

I. The ester was added to a solution of chlorine (slight excess) in carbon tetrachloride in an ordinary glass bottle, the mixture cooled off in ice water, and then placed in direct sunlight. The addition proceeded faster than with cinnamic acid, and a colorless solution was obtained in about ten minutes. On further standing in sunlight, crystals gradually separated out. These crystals were identical with cinnamic methyl ester dichloride[1] (101°), a further quantity of which was obtained on evaporation of the solvent. Only a trace of the oily addition product was present.

II. The result of the above experiment seemed to indicate that the primary addition product was allodichloride, which, by exposure to sunlight, had been converted into dichloride. The experiment was repeated, but as soon as the discoloration of the solution (eight minutes) was complete, the bottle was placed in an ice chest. Under these conditions also, the separation of the dichloride took place gradually, and its slow separation from the solution is therefore probably due to supersaturation. Only a small amount of the oily product was formed.

III. The mixture, in a brown glass bottle, was kept in an ice chest. The addition proceeded slowly; after two days there was still free chlorine, but in another two days this had disappeared. No crystals separated from the solution on standing. The solvent was distilled off under reduced pressure, and the residue placed in a vacuum desiccator in an ice chest. After three days, some crystals were deposited; these were separated from the oil by addition of carbon disulphide and filtration. From 2 grams methyl ester, only 0.2 gram of the dichloride was obtained; the oil did not solidify on long standing, and was identical with the methyl ester allodichloride prepared by Liebermann[2] from cinnamic acid allodichloride.[3]

[1] Finkenbeiner: Ber. d. chem. Ges., **27**, 890.

[2] Ber. d. chem. Ges., **28**, 2239.

[3] Liebermann (*Ibid.*, p. 2242) obtained mainly dichloride by the addition of chlorine to allocinnamic methyl ester. Unfortunately, it is not stated whether the experiment was done in the dark.

Addition of Chlorine to Cinnamyl Chloride.

Cinnamyl chloride was prepared by the action of phosphorus pentachloride on cinnamic acid; the product of the reaction was fractionated in a vacuum.[1] The chloride boils at 136°–137° under 15 mm., melts at 35°–36°, and is soluble in carbon tetrachloride and petroleum ether.

I. A solution of 5 grams chloride and the theoretical amount of chlorine in carbon tetrachloride was brought into a glass bottle, cooled in ice water, and exposed to direct sunlight. The addition proceeded quickly; in half an hour free chlorine was present only in traces. After distilling off the solvent a thick yellowish oil remained; this solidified almost entirely, on standing, to a crystalline mass. It was dried on a porous plate, and then crystallized from petroleum ether (45°). The addition product is very soluble in carbon disulphide, acetone, acetic acid, chloroform, benzene, and hot petroleum ether, moderately in cold ether, and less in cold petroleum ether. It crystallizes from the latter in prismatic needles with rounded ends, melts at 54°–55°, and is quite stable towards water; a mixture required ten hours' shaking for complete decomposition, and then gave pure cinnamic acid dichloride. Analysis:

0.1295 gram substance gave 0.2337 gram AgCl.

	Calculated for $C_6H_5.CHCl.CHCl.COCl$.	Found.
Cl	44.7	44.6

The chloride is very stable towards chlorine; in a second experiment a slight excess of chlorine was used, and the solution was not decolorized after several hours' exposure to sunlight.

II. The above experiment was repeated, using a brown bottle, and keeping the mixture in an ice chest. The addition proceeded slowly and was not completed before two days. Evaporation of the solvent yielded the theoretical amount of a yellowish oil, which could not be made to crystallize. The oil was readily soluble in carbon tetrachloride and petroleum ether, and as it gave, on decomposition with water, cinnamic acid allodichloride and dichloride, it undoubtedly consisted of a mixture of the chlorides of these stereomeric acids.

[1] Claisen and Antweiler: Ber. d. chem. Ges., **13**, 2124.

Addition of Bromine to Ethyl Cinnamate.

The following experiments were carried out in the dark, with carbon tetrachloride as a solvent. Slightly more (0.59 gram) than the theoretical amount of bromine was used. According to the previous work on this subject, these are conditions favorable for the formation of allodibromide. The variations in the experiments consisted in adding the halogen either in portions, or the full amount, to the solution of the ester (5 grams), which was kept at room temperature, or cooled off in ice water; and in the length of time the mixtures stood before they were worked up. During the experiments the mixtures were carefully excluded from exposure to light, and kept in a cool place.

I., II., and III. The mixtures were cooled in ice water, and after the bromine had been added in three portions, at intervals several hours apart, were allowed to stand a day. Yields: 14.6, 27.5, and 51.0 per cent of allodibromide.

IV., V., VI., VII., VIII., IX., and X. The halogen was added at once to the cooled solutions of ester in tetrachloride. IV. and VI. stood one day; V. and IX., three days; VII., five days; and VIII. and X., one week. The yield of oily dibromide was 14.4, 23.3, 25.4, 26.9, 31.1, 32.0, and 34.4 per cent.

XI., XII., and XIII. The solutions of ester were kept at room temperature and the halogen added in portions. XI. stood one day, and XII. and XIII., one week. Yields: 32.5, 47.3, and 49.4 per cent of oil.

XIV., XV., XVI., and XVII. As in the preceding experiments, the halogen was added only in one portion. The first three experiments stood a day, the last a week. Yields: 17.4, 28.4, 30.0, and 47.2 per cent of oil.

In these experiments, the series giving the greatest yield of allodibromide was that in which the solution was not cooled and where the halogen was added in portions; we wish to emphasize, however, that the yield of this compound depends on such subtle conditions that we do not consider our experiments as more than suggestive for future investigation. In every experiment some hydrobromic acid was obtained, but in varying amount; we could not find any connection between the relative amounts of the mineral acid and the allodibromide formed in the additions.

On standing in an ice chest, the oily dibromide deposited a small amount of the high melting dibromide, and then gradually solidified, largely to the allo product. When the crystals of the higher, with some of the lower, melting dibromide were removed from the oil, and the solid product subsequently formed was dried on a porous plate and washed with low boiling petroleum ether, it melted at 33°–35°, although it began to soften at 28°. In an earlier investigation,[1] a product melting at 28°–30° was obtained by partially melting the impure allodibromide, separating the liquid from the solid part, and repeating this operation a number of times. We endeavored to purify the allodibromide by crystallization from light petroleum ether (38°–45°), and in this way obtained a product melting at 28°–32°. It is very improbable, however, that absolutely pure allodibromide can be obtained by either of these methods.

Addition of Bromine to Methyl Cinnamate.

Michael and Whitehorne have shown that methyl cinnamate allobromide is formed in considerable proportion to the dibromide when the addition is carried out in the dark, but in view of the negative results of Sudborough and Thompson with the ethyl ester it was thought desirable to repeat this experiment.

Five grams of methyl ester were dissolved in carbon tetrachloride, the solution placed in a brown bottle, a slight excess of bromine added, and the mixture put in a closed tin box. After standing several days in an ice chest, the crystals of dibromide (116°–117°) which had separated out were removed by filtration. The filtrate, on evaporation in a vacuum, left an oil which solidified on standing. To separate the stereomeric dibromides, this product was crystallized from alcohol; the filtrate gave 1.7 grams of the allodibromide, melting at 54°–55°. A similar experiment, but using petroleum ether instead of carbon tetrachloride, gave a very much smaller yield of the allodibromide.

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[1] Michael and Whitehorne: Ber. d. chem. Ges., **34**, 3661.

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Contributions from the Kent Chemical Laboratory of the University of Chicago.

STUDIES IN CATALYSIS. I. THE CATALYSIS OF ESTERS AND OF IMIDOESTERS BY ACIDS.[1]

By Julius Stieglitz.

When an acid ester like methyl acetate is treated with water it is partially saponified, and a condition of equilibrium is ultimately established, according to the familiar equation,

$$CH_3COOCH_3 + H_2O \rightleftharpoons CH_3COOH + CH_3OH.$$

As is well known, the saponification proceeds exceedingly slowly under these conditions, but if an acid is added to the mixture, the reaction is accelerated in direct proportion to the concentration of the hydrogen ions used, and the ultimate condition of equilibrium is reached very much more rapidly. This effect of the acid or of the hydrogen ions belongs to that most interesting class of actions known as catalytic. While certain limitations and laws of catalytic action are well understood, one of the fundamental features of such actions is still largely shrouded in mystery, and that is the question as to how the catalyzer does its work. We know *what* it does, but comparatively little has been done experimentally to prove rigorously *how* it does it.

The common catalytic agents may well be divided into two or, perhaps better, three classes: (1) Purely chemical agents, such as the acids and the alkalis, acting in homogeneous mixtures; (2) Physical agents, such as finely divided platinum, colloidal metals, light rays, and the like; (3) agents which may perhaps act simultaneously both chemically and physically. Possibly some of the enzymes act in this way.

It is intended to discuss here only reactions belonging to the first class of catalytic actions, particularly the action of acids on the catalysis of acid esters. It is thought, however, that the conclusions arrived at are, in principle, equally applicable

[1] A report of the leading ideas and facts of this paper was made by the author in his address on "The Relations of Organic Chemistry to Other Sciences" before the section on Organic Chemistry of the International Congress of Arts and Science at St. Louis, September, 1904. See 4, 276 of the Report.

to the other classes of catalysis. It seems best not to attempt to give a rigorous definition of catalysis at the outset; the definition, as has often been the case, might be drawn too narrowly and thus hamper the free study of the thing itself.[1] In the case of the catalysis of the esters, we are certain of three main facts which have been proved experimentally: the action is accelerated in proportion to the concentration of the hydrogen ions present; the acid appears to remain unchanged throughout the course of the action, to remain uncombined with any of the compounds involved; and the ultimate condition of equilibrium is not measurably changed by the presence of the acid, that is, the velocities of the two reversed reactions, saponification and esterification, must be affected in a like manner and to a like degree by the presence of the acid. Whether all or any of the three characteristic features of this action may properly be considered characteristic of all catalytic actions, as is sometimes claimed, is open to question. This will become apparent below.[2]

In trying to imagine how an acid can affect the decomposition of an ester by water, we are led to recall the most fundamental property of acids, that of combining with bases and oxides to form ionizable salts. In the case under discussion we have, beside the acid, the oxide also, namely, the ester, and so we are led to the idea that an ester like methyl acetate may have basic functions and that salt formation with the acid may be the explanation of the fact of its catalysis. It was clear, at the time this idea was developed,[3] that the basic properties of an ester must be so weak that a quantitative measurement of its affinity constant and of the conditions of equilibrium of its salts could not readily be made by the methods of measurement known. Under the circumstances it was thought best to study the factors involved in a class of very closely related bodies, the imidoesters, with which quantitative measurements of all the factors could actually be carried out. The imidoesters, RC(:NH)OR′, acid esters in which the imide group (:NH) replaces the oxygen atom of the ordinary esters, are markedly basic substances which are very slowly decomposed

[1] Report of the Congress of Arts and Science, St. Louis, 4, 278 (1904).
[2] See end of Part III, p. 47.
[3] The work was started in 1898.

by water; they form well-defined salts which are very rapidly decomposed by water—the analogy appeared complete for the object of our study. There are minor differences, which will be pointed out in the proper place, but in this fundamental characteristic fact the parallelism is perfect, and the deeper the investigation was carried, the more complete the analogy between the two classes appeared to be.

The study of the action of water on the imidoesters and their salts has been carried out with Messrs. I. H. Derby, W. Mc Cracken, and H. I. Schlesinger. In other papers they will present, in detail, the experimental results on a large number of imidoesters; at the present moment it is desired only to present the theoretical discussion of the questions at issue, to give the main results established by experiment, and to draw the necessary conclusions as to the nature of the catalysis of imidoesters and of ordinary esters.[1]

I. The Decomposition of the Imidoesters.

When methyl imidobenzoate is dissolved in water, it is very slowly decomposed, giving almost entirely methyl alcohol and benzonitrile, according to[2]

$$C_6H_5C(NH)OCH_3 \rightarrow C_6H_5CN + CH_3OH \qquad (1).$$

To a minimal extent only, it forms methyl benzoate and ammonia, according to[3]

$$C_6H_5C(NH)OCH_3 + H_2O \rightarrow C_6H_5COOCH_3 + NH_3 \qquad (2).$$

Both reactions are practically nonreversible under the conditions of the experiment. The addition of hydrochloric acid to the solution enormously increases the velocity of the second reaction, and this may become practically the exclusive reaction. The acid forms the hydrochloride with the base, but, as an imidoester is a very weak base, we have, in an aqueous solution of its hydrochloride, partial hydrolysis of the salt, and a condition of equilibrium is established, according to

$$C_6H_5C(NH_2Cl)OCH_3 + H_2O \rightleftarrows C_6H_5C(NH_2OH)OCH_3 + HCl \qquad (3).$$

[1] I wish to take this opportunity to thank my young collaborators for their faithful work and valuable assistance. All the experimental work was carried out by them under my guidance.

[2] See Schlesinger's article.

[3] The experimental proof of this was recently brought out by Miss Edith E. Barnard.

In such a solution it may be the salt or its positive ion thta is undergoing the rapid saponification, it may be the free base, or it may be all indifferently. A quantitative investigation of the relations promised to give a conclusive answer to the question as to just how the acid accelerates so decidedly reaction (2), whether by its mere presence or rigorously by the formation of the salt or its positive ion. It may be stated at once that the experimental results prove conclusively that the reacting substance which gives ammonia and a benzoic ester is, as was expected, only the salt or, rather, *only its positive ion*, and that the accelerating action of the acid is simply due to the formation of *larger reacting masses of the active ion from the scarcely ionized, weak base.*

From the results of Messrs. Derby, McCracken, and Schlesinger it also appears that the decomposition of imidoesters by water under the influence of acids is subject, *like that of the ordinary esters*, to an accelerating "salt-effect," due, most likely,[1] to the effect of the presence of many ions on the *ionization* of *water* which enters into the reaction (equation 2). The material gathered relative to this fact being rather fragmentary, the investigation of this "effect" and of the closely related question of the effect of the presence of nonionized substances has been carried on by Miss Barnard. Her work has shown that again, as in the catalysis of acid esters, nonionized substances have no effect on the velocity of the action between imidoester salts and water, but electrolytes have a decided "salt effect." Later papers will present the results in detail.

It was also found in the work of Mr. Schlesinger that the decomposition into nitrile and alcohol according to reaction (1) is enormously accelerated, proportionately to the concentration of the hydroxyl ions used, by the addition of alkalis. This brought out a further line of analogy between the imidoesters and the acid esters. As will be shown and fully discussed by Schlesinger in a later paper, the accelerating effect of the alkali is considered, by analogy with the proved explanation of the catalytic effect of the acids, to be due to very weak acid properties of the imido-

[1] Euler: Z. physik. Chem., **33**, 348 (1900).

esters (they are amphoteric), the alkali producing an increase in the concentration of the *negative ions*, which form the *reacting mass in the decomposition into nitrile and alcohol* according to equation (1).

From studies of the decomposition of an imidoester in a purely aqueous solution, carried out with Derby and with Schlesinger, it appears that the *nonionized molecules* of the imidoesters also break down to nitrile and alcohol, but with a velocity constant which is exceedingly small as compared with that for the decomposition of the negative ions.

We have, therefore, the following three simultaneous decomposition reactions for an imidoester, each proceeding according to an established velocity constant:

(I.) $C_6H_5C(:\overset{+}{N}H_2)OCH_3 + H_2O \rightarrow C_6H_5COOCH_3 + \overset{+}{N}H_4$,

(II.) $C_6H_5C(:\overset{-}{N})OCH_3 \rightarrow C_6H_5CN + \overset{-}{O}CH_3$,

(III.) $C_6H_5C(NH)OCH_3 \rightarrow C_6H_5CN + HOCH_3$.

The theoretical significance of these results for the question of catalytic action, and their application to the catalysis of ordinary esters, will be discussed in Part III., after the presentation in Part II. of the mathematical treatment of the problem with a condensed summary of some of the experimental results.

II. The Velocity of Decomposition of Imidoesters by Aqueous Acids.

The reaction which is accelerated by the addition of an acid to an imidoester, as explained above, is its decomposition by water into ammonia and an acid ester, according to

$$RC(NH)OR' + H_2O \rightarrow RCOOR' + NH_3 \qquad (2).$$

A salt is formed which is partially hydrolyzed, according to

$$RC(:NH_2Cl)OR' + H_2O \rightleftarrows RC(NH_2OH)OR' + HCl \qquad (3).$$

It was early observed that the salts of the weaker bases, which are more highly hydrolyzed into the free base and the acid, were also most rapidly decomposed according to reaction

(2). In such a solution, then, the substance actually undergoing this decomposition might be the base and salt indifferently, the free base present, or only the salt (its positive ions). These three possibilities are expressed in the equations

$$\frac{dx}{dt} = k_{subst} \times C_{subst} \qquad \text{(I.)},$$

$$\frac{dx}{dt} = k_{base} \times C_{base} \qquad \text{(II.)},$$

$$\frac{dx}{dt} = k_{salt} \times C_{salt} \qquad \text{(III.)},$$

in which C_{subst}, C_{base}, and C_{salt} are functions of x and always represent the concentration of the substance indicated at the moment t.

For the last case, in the presence of considerable amounts of the free base, we would have, rigorously, also the possibility of the rapid decomposition of the salt or its ions, according to equation (2), occurring simultaneously with the very slow decomposition of the nonionized free base according to reaction (1) (p. 31), which might take place at the same rate as it does in the absence of any acid. We would have then

$$\frac{dx}{dt} = k_{salt} \times C_{salt} + k'_{base} \times C_{base} \qquad \text{(III'.)},$$

where k_{salt} is the velocity constant of equation (III.) and k'_{base} is the velocity constant of the transformation of the base into benzonitrile and an alcohol according to (I.), as determined in Part VII.[1] Where the amount of the free base is small, the velocity of its transformation being also exceedingly small, (III.) may be substituted for (III'.) as expressing the course of the mixed reaction.

In order to test these possibilities, it was necessary to determine two things experimentally: first, the actual change x in time t; and, second, the proportion of salt, free base, and acid present at any moment t. The rate of change was determined by simple alkalimetric titration methods which will be described in the reports of my collaborators. In regard to the

[1] See a later paper.

second point, considering the equilibrium equation (3), we have for the free weak base present

$$C_{pos.\,ion} \times C_{OH} = k_{base} \times C_{base} \qquad (4).$$

For dilute solutions at 25°,

$$C_H \times C_{OH} = k_{H_2O} = 1.2 \times 10^{-14} \qquad (5),^1$$

and consequently,

$$\frac{C_{pos.\,ion}}{C_{base} \times C_H} = \frac{k_{base}}{k_{H_2O}} = k_{hydrolysis} \qquad (6).$$

In dilute solutions the salt and the free strong acid, hydrochloric acid, are proportionately and practically completely ionized, while the base is present in nonionized form; so we may write (6)

$$\frac{C_{salt}}{C_{base} \times C_{acid}} = \frac{k_{base}}{k_{H_2O}} = k_{hydrolysis} \qquad (6'),$$

which is Walker's[2] fundamental equation for a hydrolyzed salt solution, as developed by Arrhenius.[3]

$k_{hydrolysis}$ was determined for a number of imidoester salts by conductivity measurements of the solutions. A few of the results follow:

	$k_{hydrolysis.}$
Methyl imidobenzoate	4×10^5
Ethyl "	9.1×10^5
Methyl imido-*m*-nitrobenzoate	5.8×10^4
Ethyl "	8×10^4

With the aid of these constants the equations (I.), (II.), (III.), and (III.′) may be solved.

(1) Equation (I.), $\frac{dx}{dt} = k_{subst} \times (C - x)$,

represents a simple reaction of the first order, the whole substance taking part in the action, base and salt indifferently.

[1] Van't Hoff: "Theoretical and Physical Chemistry," I, 133.
[2] Z. physik. Chem., **4**, 319 (1889).
[3] *Ibid.*, **5**, 19 (1890).

We have, then,

$$k_{subst} = \frac{1}{t_2 - t_1} \log \text{nat} \frac{C - x_1}{C - x_2} \qquad (7).$$

(2) Equation (II.), $\frac{dx}{dt} = k_{base} \times C_{base}$,

represents the velocity of the reaction as being proportionate only to the concentration of the free base present at any moment. We will call the total original concentration of the imidoester used, both as hydrochloride and as free base, 1 gram molecule in V liters, and the known original concentration of the salt (hydrochloride) of the imidoester used, s gram molecules in V liters. The concentration of the free acid formed by hydrolysis of the salt at any moment t shall be called y gram molecules in V liters, and the amount of imidoester saponified in t minutes, x gram molecules in V liters. Then, at any moment, we have[1]

$$C_{acid} = \frac{y}{V}, \quad C_{salt} = \frac{s - x - y}{V}, \quad C_{base} = \frac{1 - s + y}{V}.$$

Inserting these values in equation (6′), we obtain

$$\frac{s - x - y}{V} = k_{hydrolysis} \times \frac{1 - s + y}{V} \times \frac{y}{V} \qquad (6').$$

For a given experiment, V is a constant. Putting in $K_v = \frac{V}{k_{hydrolysis}}$ and solving for y, we have

$$y = -\frac{1 - s + K_v}{2} + \sqrt{\left(\frac{1 - s + K_v}{2}\right)^2 + K_v(s - x)} \quad (8).$$

Substituting this value in the expression for C_{base} we have

$$C_{base} = \frac{1}{V}\left[\frac{1 - s - K_v}{2} + \sqrt{\left(\frac{1 - s + K_v}{2}\right)^2 + K_v(s - x)}\right] \quad (9).$$

[1] The imidoesters are such weak bases, compared with ammonia, that the amount of ammonium chloride decomposed by the little free ester present was considered a negligible quantity. The affinity constants are

$$k_{NH_3} = 2 \times 10^{-5}, \quad \text{and} \quad k_{im.est} = 5 \times 10^{-9}$$

and less.

Then equation (II.) becomes

$$\frac{d\frac{x}{v}}{dt} = k_{base} \times \frac{1}{V}\left[\frac{1-s-K_v}{2} + \sqrt{\left(\frac{1-s+K_v}{2}\right)^2 + K_v(s-x)}\right] \quad (10),$$

$$t = \frac{2}{k_{base}} \int \frac{dx}{1-s-K_v + \sqrt{(1-s+K_v)^2 + 4K_v(s-x)}} \quad (11).$$

Integrating this expression, we obtain

$$k_{base} = \frac{1}{K_v(t_2-t_1)}\left[\sqrt{R-4K_vx_1} - \sqrt{R-4K_vx_2} + (1-s-K_v) \text{ log nat } \frac{\sqrt{R-4K_vx_2} + (1-s-K_v)}{\sqrt{R-4K_vx_1} + (1-s-K_v)}\right] \quad (12),$$

in which $R = (1-s+K_v)^2 + 4K_vs$.

When the hydrochloride of an imidoester is used alone, without an excess of free base, then the free base formed by hydrolysis of the salt has the same concentration as the free acid; for this special, but in practice more common, case, $s = 1$, and the above expression becomes

$$k_{base} = \frac{1}{t_2-t_1}\left[\sqrt{1 + \frac{4(1-x_1)}{K_v}} - \sqrt{1 + \frac{4(1-x_2)}{K_v}} + \text{log nat } \frac{\sqrt{K_v^2 + 4K(1-x_1)} - K_v}{\sqrt{K_v^2 + 4K_v(1-x_2)} - K_v}\right] \quad (12').$$

Owing to the very small value of K_v, we may simplify this and use

$$k_{base} = \frac{2}{(t_2-t_1)\sqrt{K_v}}\left[\sqrt{1-x_1} - \sqrt{1-x_2}\right] \quad (12'').$$

(3) Equation (III.), $\frac{dx}{dt} = k_{salt} \times C_{salt}$, represents the velocity of the decomposition of imidoesters into ammonia and esters under the influence of acids as directly proportionate to the concentration of the salt present or, for our work in dilute solu-

tions, to that of the positive ions of the imidoesters present at any moment. If we use the same symbols as in (2) to represent the concentrations we find

$$C_{salt} = \frac{s-x-y}{V}$$

$$= \frac{1}{V}\left[s-x+\frac{1-s+K_v}{2} - \sqrt{\left(\frac{1-s+K_v}{2}\right)^2 + K_v(s-x)}\right] \quad (13).$$

Substituting this value in (III.), we obtain

$$\frac{d\frac{x}{v}}{dt} = k_{salt} \times \frac{1}{V}\left[s-x+\frac{1-s+K_v}{2} - \sqrt{\left(\frac{1-s+K_v}{2}\right)^2 + K_v(s-x)}\right] \quad (14),$$

and

$$t = \frac{1}{k_{salt}}\int_a^{\quad} \frac{dx}{s-x+\frac{1-s+K^v}{2} - \sqrt{\left(\frac{K_v}{2}\right)^2 + (s-x)K_v}} \quad (15).$$

Integrating, we find

$$k_{salt} = \frac{1}{t_1 - t_1}\left[\frac{1-s+K_v}{1-s} \log \text{nat} \frac{\sqrt{R-4K_vx_1}-(1-s+K_v)}{\sqrt{R-4K_vx_2}-(1-s+K_v)} + \frac{1-s-K_v}{1-s} \log \text{nat} \frac{\sqrt{R-4K_vx_1}+(1-s-K_v}{\sqrt{R-4K_vx_2}+(1-s-K_v}\right] \quad (16),$$

in which expression $R=(1-s+K_v)^2+4K_vs$.

In the calculations, K_v having a very small value, the factors before the logarithms can be dropped.

For the case in which we use the hydrochloride of an imidoester without an excess of the free base, and $s=1$, the above expression becomes indefinite. But for this case, we have

$$C_{salt} = \frac{1}{V}\left[1-x+\frac{K_v}{2} - \sqrt{\left(\frac{K_v}{2}\right)^2 + (1-x)K_v}\right] \quad (17).$$

Integrating the corresponding differential equation, we find

$$k_{sa} = \frac{1}{t_2 - t_1}\left[\log\text{nat}\,\frac{2-2x_1+K_v-\sqrt{K_v^2+4K_v(1-x_1)}}{2-2x_2+K_v-\sqrt{K_v^2+4K_v(1-x_2)}} - \frac{1}{\sqrt{\frac{1-x_1}{K_v}+0.25}-0.5} + \frac{1}{\sqrt{\frac{1-x_2}{K_v}+0.25}-0.5}\right] \quad (18).$$

Discarding the functions which do not affect the arithmetical results, we have, more simply,

$$k_{salt} = \frac{1}{t_2 - t_1}\left[\log\text{nat}\,\frac{1-x_1-\sqrt{(1-x_1)K_v}}{1-x_2-\sqrt{(1-x_2)K_v}} - \sqrt{\frac{K_v}{1-x_1}}+\sqrt{\frac{K_v}{1-x_2}}\right] \quad (18').$$

For less rigorous calculations, when the salts are used *without an excess of free base*, the degree of hydrolysis being very small, we can consider practically the whole substance to be salt, and use, more simply,

$$k_v = \frac{1}{t_2 - t_1}\log\text{nat}\,\frac{C-x_1}{C-x_2}.$$

(4) If we wish to take into consideration the simultaneous saponification of the imidoester salt into ammonia and an acid ester and the decomposition of the free base, at a very much slower rate (see Part VII.), into alcohol and a nitrile, we would have

$$\frac{dx}{dt} = k_{salt}\,C_{salt} + k_{base}\,C_{base} \qquad (III'),$$

where k_{salt} is the velocity constant for the saponification of the salt or positive ion of the imidoester, and k_{base} is the constant determined in Part VII. for the decomposition of the non-ionized free base into a nitrile and an alcohol, provided the decomposition of the base remains unaffected by the presence of the salt. The results obtained indicate that such is the case. If we use the same symbols as in (2) and (3), C_{salt} has the value given in equation (13); C_{base}, that given in equation (9).

Then

$$\frac{d\frac{x}{v}}{dt} = k_{salt}\frac{1}{V}\left[s - x + \frac{1-s+K_v}{2} - \sqrt{\left(\frac{1-s+K_v}{2}\right)^2 + K_v(s-x)}\right] + k_{base}\frac{1}{V}\left[\frac{1-s-K_v}{2} + \sqrt{\left(\frac{1-s+K_v}{2}\right)^2 + K_v(s-x)}\right] \quad (19).$$

$$t = \int_0^{} \frac{dx}{k_{salt}\left[s-x+\frac{1-s+K_v}{2} - \sqrt{\left(\frac{1-s+K_v}{2}\right)^2 + K_v(s-x}\right] + \frac{dx}{k_{base}\left[\frac{1-s-K_v}{2} + \sqrt{\left(\frac{1-s+K_v}{2}\right)^2 + K_v(s-x)}\right]}} \quad (20).$$

Integrating, we obtain

$$t_2 - t_1 = \frac{1-s-K_v}{k_{salt} - sk_{salt} - K_v k_{base}} \times \text{log nat}\frac{\sqrt{R-4K_v x_1} + (1-s-K^v)}{\sqrt{R-4K_v x_2} + (1-s-K_v)} + \frac{k_{salt}(1-s+K_v) - 2K_v k_{base}}{k_{salt}(k_{salt} - sk_{salt} - K_v k_{base})} \times \text{log nat}\frac{\sqrt{R-4K_v x_1} - (1-s+K_v) + \frac{2K_v k_{base}}{k_{salt}}}{\sqrt{R-4K_v x_2} - (1-s+K_v) + \frac{2K_v k_{base}}{k_{salt}}} \quad (21),$$

in which $R = (1-s+K_v)^2 + 4K_v s$.

Some of the functions can be dropped in the application, as not affecting the numerical result; we have, more simply,

$$t_2 - t_1 = \frac{1}{k_{salt}} \times \text{log nat}\frac{\sqrt{R-4K_v x_1} - (1-s+K_v) + \frac{2K_v k_{base}}{k_{salt}}}{\sqrt{R-4K_v x_2} - (1-s+K_v) + \frac{2K_v k_{base}}{k_{salt}}} \quad (21').$$

The expression $\frac{2K_1k_{base}}{k_{salt}}$ in the logarithmic term must be calculated by using the constant k_{salt} as previously determined in the absence of an excess of the free base, and the constant k_{base} as determined in Part VII. for the base in the absence of the salt.

In the following tables sufficient of the experimental results will be summarized to enable us to distinguish between the above possibilities, and to recognize sharply the actual reacting substance in the formation of ammonia and an alkyl benzoate when an imidoester is decomposed by water in the presence of dilute acid.

In the first table are given constants calculated according to the equations (12′) and (12) to see if the velocity of the reaction is proportionate to the concentration of the free base always present. Each series of numbers in a line following k_{base} represents the results at different time intervals of one experiment. Under the groups marked (*a*) are given experiments with the hydrochlorides of the imidoesters present alone, the free base present being formed wholly by the hydrolytic dissociation of the salts by water; under (*b*) are given the results of experiments with the hydrochlorides in the presence of an added excess of the free bases.

Table I.

(1) *Methyl Imidobenzoate*, $C_6H_5C(:NH)OCH_3$.

(*a*) 0.05 molar salt, at 25°,[1] total time, 400 minutes.

$10^3\ k_{base}$: 771; 676; 560; 460.

(*b*) 0.05 molar salt, 0.0125 molar free base, 25°, 180 minutes.

$10^3\ k_{base}$: 19.5; 16.5; 15.1; 12.9.

0.05 molar salt, 0.01 molar free base, 25°, 445 minutes.

$10^3\ k_{base}$: 20.1; 16.0————10.15.

(2) *Ethyl Imidobenzoate*, $C_6H_5C(NH)OC_2H_5$.

(*a*) 0.05 molar salt, 25°, 720 minutes.

$10^3\ k_{base}$: 620; 597; 560; 513; 437.

(*b*) 0.0375 molar salt, 0.0125 molar base, 25°, 250 minutes.

$10^3\ k_{base}$: 458; 429; 400; 413; 385.

[1] The temperature was always kept constant within ± 0.01°, unless otherwise stated.

Table I—(Continued).

(3) *Methyl Imido-m-nitrobenzoate*, $NO_2C_6H_4C(NH)OCH_3$.

(*a*) 0.05 molar salt, 18°, 108 minutes.

$10^3\ k_{base}$: 1170; 1014; 782; 692.

(*b*) 0.05 molar salt, 0.005 molar base, 18°, 107 minutes.

$10^3\ k_{base}$: 194; 146; 104.

It is obvious that k_{base} is not a constant in any series and not constant for the same reaction under varying original concentrations of the free base. Evidently the reaction is not a function of the concentration of the free imidoester.[1]

In Table II. are given some of the constants, k_{subst}, calculated according to equation (7) to see if the velocity of the reaction is proportionate to the total substance present, salt and base indifferently. When salts are used alone (Series *a*), the degree of hydrolysis being very small (usually only a very few per cent of the substance), there is not sufficient difference between the concentrations of the salt and the total substance to appear in the calculations to any extent; if the one gives a real constant, the other will also. But a sharp distinction can be made by comparing these constants (Series *a*) with those obtained in Series (*b*) where the salt and an excess of the free base are used; in these cases there is, of course, a decided difference in the concentration of the salt and the total substance.

Table II.

(1) *Methyl Imidobenzoate*, $C_6H_5C(NH)OCH_3$.

(*a*) 0.025 molar hydrochloride, 25°, 390 minutes.

$10^5\ k_{subst}$: (520); (610); 587; 582; 580; 576; 578; 576. Mean: 580.

0.05 molar hydrochloride, 25°, 440 minutes.

$10^5\ k_{subst}$: 557; 569; 539; 523; 514; 534. Mean: 539.

0.05 molar hydrochloride, 25°, 400 minutes.

$10^5\ k_{subst}$: (589); 548; 543; 536; 543; 541. Mean: 542.

[1] Reactions in which the free bases in hydrolyzed salt solutions were found to be the only reacting ingredient were described in THIS JOURNAL, **31**, 458 (1904) by Stieglitz and Upson.

Table II—(Continued).

(*b*) 0.05 molar hydrochloride, 0.0125 molar base, 25°, 180 minutes.

$10^5\ k_{subst}$: 465; 424; 421; 396.

0.04 molar salt, 0.01 molar base, 25°, 420 minutes.

$10^5\ k_{subst}$: 532; 463; 438; 403; 387; 375; 364; 318.

(2) *Ethyl Imidobenzoate*, $C_6H_5C(NH)OC_2H_5$.

(*a*) 0.05 molar hydrochloride, 25°, 620 minutes.

$10^5\ k_{subst}$: 313; 310; 314; 320. Mean: 314.

0.05 molar salt, 25°, 300 minutes.

$10^5\ k_{subst}$: 309; 318; 309. Mean: 312.

0.05 molar salt, 25°, 540 minutes.

$10^5\ k_{subst}$: 304; 302; 306; 304; 306. Mean: 304.

0.05 molar salt, 25°, 570 minutes.

$10^5\ k_{subst}$: (266); 302; 302; 304; 304. Mean: 303.

(*b*) 0.0375 molar salt, 0.0125 molar base, 25°, 250 minutes.

$10^5\ k_{subst}$: 226; 221; 216.

(3) *Methyl Imido-m-nitrobenzoate*, m-$NO_2C_6H_4C(NH)OCH_3$.

(*a*) 0.05 molar salt, 18°, 108 minutes.

$10^4\ k_{subst}$: 251; 251; 250; 241; 245; 238; 239; 237. Mean: 244.

0.025 molar salt, 18°, 109 minutes.

$10^4\ k_{subst}$: 251; 246; 239; 249; 243; 240; 234; 234. Mean: 242.

(*b*) 0.05 molar salt, 0.005 molar base,[1] 18°, 67 minutes.

$10^4\ k_{subst}$: 235; 225; 221; 214; 207; 201.

The contrast in the values of the series (*a*) and (*b*) for each ester, and a survey of the results obtained in a single long experiment of Series (*b*) (*e. g.*, experiment 1*b*), show positively that the velocity of the reaction under discussion is not proportionate to the concentration of the total substance present.

In the third table are given the constants calculated according to equations (16), (18′), and (21′), to see if the velocity of the reaction is proportionate simply to the concentration of the salt present. The series under (*a*) represent again velocities where pure salts were used, under (*b*) are given the constants for experiments in which an excess of free base is present, k_{salt}

[1] This free base is very difficultly soluble.

representing the constant calculated according to equation (16) without any correction for the simultaneous, exceedingly slow decomposition of the free base into a nitrile and an alcohol, and k'_{salt} representing the constant calculated according to equation (21′) where it is assumed that the free base is decomposing very slowly of itself, exactly as it does in the absence of the salt, according to the constant for this reaction determined in Part VII.

Table III.

(1) *Methyl Imidobenzoate*, $C_6H_5C(NH)OCH_3$.

(*a*) 0.025 molar salt, 25°, 390 minutes.

$10^5\ k_{salt}$: (527); (669); 610; 600; 595; 590; 592; 590. Mean: 596.

0.05 molar salt, 25°, 440 minutes.

$10^5\ k_{salt}$: 560; 573; 543; 530; 520; 541; 538. Mean: 544.

0.05 molar salt, 25°, 400 minutes.

$10^5\ k_{salt}$: 592; 550; 548; 541; 550; 550. Mean: 555.

(*b*) 0.05 molar salt, 0.0125 molar base, 25°, 180 minutes.

$10^5\ k_{salt}$: 603; 552; 608; 584. Mean: 587.

$10^5\ k'_{salt}$: 593; 543; 596; 571. Mean: 576.

0.04 molar salt, 0.01 molar base, 25°, 429 minutes.

$10^5\ k_{salt}$: 553; 566; 585; 598; 616; 579; 605. Mean: 586.

$10^5\ k'_{salt}$: 545; 558; 571; 580; 591; 560; 570. Mean: 566.

Mean, Series (*a*): $k_{salt} = 565$.

Mean, Series (*b*): $k_{salt} = 586$, $k'_{salt} = 571$.

(2) *Ethyl Imidobenzoate*: $C_6H_5C(NH)OC_2H_5$.

(*a*) 0.05 molar salt, 25°, 620 minutes.

$10^5\ k_{salt}$: 313; 312; 316; 323. Mean: 316.

0.05 molar salt, 25°, 300 minutes.

$10^5\ k_{salt}$: 310; 320; 310. Mean: 313.

0.05 molar salt, 25°, 540 minutes.

$10^5\ k_{salt}$: 306; 304; 307; 306; 307. Mean: 306.

0.05 molar salt, 25°, 570 minutes.

$10^5\ k_{salt}$: 310; 304; 304; 306; 306. Mean: 306.

(*b*) 0.0375 molar salt, 0.0125 molar base, 25°, 250 minutes.

$10^5\ k_{salt}$: 287; 299; 305. Mean: 297.

Mean, Series (*a*): $k_{salt} = 310$. Series (*b*): $k_{salt} = 297$.

Table III—(Continued).

(3) *Methyl Imido-m-nitrobenzoate.* m-$NO_2C_6H_4C(NH)OCH_3$.

(*a*) 0.05 molar salt, 18°, 108 minutes.

$10^4\,k_{salt}$: 259; 258; 261; 256; 253; 251; 253; 252. Mean: 255.

0.025 molar salt, 18°, 109 minutes.

$10^4\,k_{salt}$: 264; 259; 253; 265; 259; 258; 253; 256. Mean: 258.

(*b*) 0.05 molar salt, 0.005 molar base, 18°, 67 minutes.

$10^4\,k_{salt}$: 265; 258; 259; 257; 256; 258. Mean: 259.

$10^4\,k_{salt}$: 268; 260; 261; 258; 257; 2623. Mean: 261.

Mean, Series (*a*): $k_{salt} = 257$. Series (*b*): $k_{salt} = 259$, $k'_{salt} = 261$.

The agreement in the results for the constants obtained in each experiment shows that they represent real constants. The comparison of the constants obtained for a given ester in the presence or the absence of an excess of free base shows also that the reaction velocity in all cases is strictly proportionate to the concentration of the salt (the positive ions) present at any moment; thus, for methyl imidobenzoate (Series 1), the mean velocity constant in the absence of an excess of the free base is $k_{salt} = 0.00565$; in the presence of the free base, $k_{salt} = 0.00585$ or $k'_{salt} = 0.00571$, respectively, according to whether or not a correction is made for the simultaneous, very slow decomposition of the free base in a different direction. For ethyl imidobenzoate the average constants are $k_{salt} = 0.00310$ and $k_{salt} = 0.00297$; for methyl imido-*m*-nitrobenzoate the averages are $k_{salt} = 0.0257$ and $k_{salt} = 0.0259$ and $k'_{salt} = 0.0261$.

From Tables I., II., III., which represent only a part of many similar experiments leading to the same conclusion, it appears certain, therefore, that the addition of hydrochloric acid, which so greatly accelerates the velocity of saponification of an imidoester into ammonia and an ester does so simply through salt formation, that is, the salt decomposes very much faster in this direction than the free base does. In the dilute solutions used, practically all of the salt is ionized and so it is obvious that it is the positive ion which is the active constituent,

reacting with water with a constant velocity at a given temperature.[1] In the aqueous solution of the free base, we have a very few of these positive ions, so few, however, that their decomposition is barely discernible as compared with the decomposition of the nonionized base, which is present in largest quantity and which gives, according to equation (1), a nitrile and an alcohol. The addition of an acid, with the formation of easily ionizable salts, greatly increases the concentration of the positive ions, and their reaction with water, expressed in equation (2), leading to the formation of an ester and ammonium ions, becomes the predominating one. We must therefore write the reaction as

$$CH_3C(\overset{+}{N}H_2)OCH_3 + H_2O \rightarrow C_6H_5COOCH_3 + \overset{+}{N}H_4 \quad (2')$$

The accelerating, or let us call it the catalytic, action of the hydrochloric acid has, then, been proved to be due in this case simply to the formation of positive ions, that is, to the formation of different molecules of different energy content and of greater reactivity or instability. Now, if this should prove to be the correct explanation of the catalytic actions of acids in general, it is obvious that by this same power of forming salts and positive ions they should be liable, also, in certain cases to *retard* action instead of accelerating it, provided the positive ion or salt is less *reactive or more stable* than the free base. That must be a consequence of this theory and we already have brought out its complete experimental confirmation and elaboration in the work carried out with Dr. Upson on the rearrangement of the aminophenylalkyl carbonates,[2] an investigation which was undertaken expressly in order to test rigorously the correctness of this conclusion.[3] As that investigation forms a part of the present argument, it is desired to incorporate in a very brief summary the most important results of the work. The aminophenylalkyl carbonates rearrange spontaneously into oxyphenylurethanes, according to

[1] Dr. Schlesinger's work on the velocities of the reactions and the degrees of ionization of the salts used, completed (1905) since the writing of this (1904), fully confirms the conclusion that only the ions of the salt are decomposed by water, as will be described in one of the next papers.

[2] This Journal, **31**, 458 (1904).

[3] *Ibid.*, 461.

$$NH_2C_6H_4OCO_2C_2H_5 \longleftarrow C_2H_5O_2CNHC_6H_4OH \quad (22),$$

by a shifting of the carbethoxyl group from the oxygen to the nitrogen atom.

The hydrochlorides of these amines are hydrolyzed in aqueous solution according to

$$ClH_3NC_6H_4OCO_2C_2H_5 + H_2O \rightleftarrows HOH_3NC_6H_4OCO_2C_2H_5 + HCl \quad (23).$$

Hydrochloric acid retards, but does not prevent, the rearrangement expressed in (22), and it was suspected that it retards it quantitatively by salt formation only; that in the aqueous solution of the salts the rearrangement would still proceed in rigorous proportion to the concentration of the small amount of free base present according to (23) and would ultimately complete itself. The experimental results proved that such is actually the case, the action being followed with six bases through ten hours and the velocity remaining constantly proportionate to the small concentration of the free base in the presence of the continually accumulating acid.

Briefly, then, hydrochloric acid has been shown to accelerate or retard action quantitatively *through salt or ion formation. Now these enormous changes in speeds of reaction are really the main characteristic of catalytic action*; it remains, however, to determine whether the two other characteristics important for *certain* cases, are also in agreement with this conception, rigorously applied; first, that the catalyzer need not appear to enter into combination with any of the substances present and, second, that in a reversible reaction it need not measurably change the final condition of equilibrium. We shall now test this view by the rigorous application of the above principle of salt or, rather, ion formation to the well-known catalysis of methyl acetate, to which the last two characteristics mentioned are known to apply.

III. The Catalysis of Methyl Acetate.

The intimate connection of this case with the work on the imidoesters is readily recognized as follows: we found above that for imidoesters,

$$\frac{dx}{dt} = k \times C_{pos.\ ion.} \qquad \text{(III.)}.^{1}$$

But

$$C_{pos.\ ion.} = K_{hydrolysis} \times C_{base} \times C_H \qquad (6),^{2}$$

and therefore

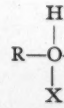
$$\frac{dx}{dt} = k \times K_{hydrolysis} \times C_{base} \times C_H \qquad (24),$$

$$= k' \times C_{base} \times C_H \qquad (24').$$

But this is the well-known velocity equation for the catalysis of esters in the presence of an acid, C_{ester} being substituted for C_{base},

$$\frac{dx}{dt} = k \times C_{ester} \times C_H \qquad (25),$$

and so, if the ester could form salts with an acid, its saponification could undoubtedly be due to the decomposition of its positive ions by water. This important link in the argument has been supplied, since the work was first undertaken, by the discoveries by Baeyer[3] and others that esters do combine with acids to give compounds, which, though very unstable, are unmistakable salts. They are almost certainly oxonium salts, possibly, but less likely,[4] carbonium salts; either conception will do for the application of our conclusions, and we shall use the much more likely view that they are oxonium salts,



It may be added that Coehn[5] has proved that these compounds are true salts, capable of ionization, by showing that in a solution of dimethylpyrone in hydrochloric acid the pyrone migrates, under the influence of an electric current, to the negative pole as a positive ion of an oxonium base. It may also

[1] Pages 34 and 46.
[2] Page 35.
[3] Ber. d. chem. Ges., **34**, 2679 (1901), etc.
[4] Stieglitz and Edith Barnard: J. Am. Chem. Soc., **27**, 1016 (1905).
[5] Ber. d. chem. Ges., **35**, 2673 (1902).

be recalled that methyl acetate gives with hydrogen chloride, in the absence of water, methyl chloride, exactly as the hydrochlorides of the imidoesters do when they are heated to 100°–130° in the absence of water.

Methyl acetate must then form with water an oxonium base in the same way that ammonia combines with water to form ammonium hydroxide,

$$(CH_3CO)OCH_3 + HOH \rightleftharpoons (CH_3CO)-\underset{\displaystyle OH}{\overset{\displaystyle H}{\underset{|}{\overset{|}{O}}}}-CH_3 \quad (26),$$

and

$$C_{ester} \times C_H \times C_{OH} = k' \times C_{base} \qquad (27).$$

The base ionizes according to

$$(CH_3CO)-\underset{\displaystyle H}{\overset{\displaystyle OH}{\underset{|}{\overset{|}{O}}}}-CH_3 \rightleftharpoons (CH_3CO)-\overset{+}{\underset{\displaystyle H}{\underset{|}{O}}}-CH_3 + \bar{O}H \quad (28),$$

for which we have

$$C_{est.\ pos.\ ion} \times C_{OH} = k_{base} \times C_{base} \qquad (29).$$

Combining (27) and (29), we have

$$C_{est.\ pos.\ ion} = \frac{k_{base}}{k'} \times C_{ester} \times C_H \qquad (30).^1$$

Now, if, as was proved for the imidoesters, it is only the positive ions which react with water to give acetic acid and methyl alcohol, according to the fundamental equation

$$CH_3COOCH_3 + HOH \rightarrow CH_3COOH + CH_3OH \quad (31),$$

we would have for the velocity of this reaction of saponification

$$\frac{dx}{dt} = k_s \times C_{est.\ pos.\ ion} \times C_H \times C_{OH} \qquad (32).^2$$

For water,

$$C_H \times C_{OH} = k_w \times C_{H_2O} \qquad (33).$$

[1] See footnote, page 50.

[2] $C_{est.\ pos.\ ion}$ is a function of x.

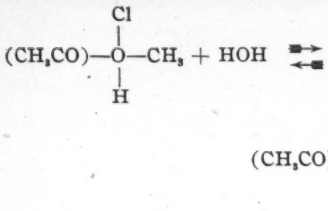
Substituting the values of (30) and (33) in (32), we have

$$\frac{dx}{dt} = k_s \times \frac{k_{base}}{k'} \times C_{ester} \times C_H \times k_w \times C_{H_2O} \quad (34),$$

$$= K_s \times C_{ester} \times C_{H_2O} \times C_H \quad (34'),$$

as representing the velocity of the decomposition of methyl acetate by water in the absence of any acid.

If we add hydrochloric acid to the mixture of methyl acetate and water, we obtain the hydrochloride of the oxonium base, but the salt is almost completely hydrolyzed according to the equation



In such a solution we would have for the free base present,[1] according to (27), (29), and (30),

$$C'_{est.\ pos.\ ion} = \frac{k_{base}}{k'} \times C_{ester} \times C'_H \quad (36).$$

Substituting the new value for $C_{est.\ pos.\ ion}$ in the velocity equation (32), we have, with the aid of (33), for the velocity of decomposition of methyl acetate in the presence of hydrochloric acid,

$$\frac{dx}{dt} = k_s \times \frac{k_{base}}{k'} \times C_{ester} \times C'_H \times k_w \times C_{H_2O} \quad (37),$$

$$= K_s \times C_{ester} \times C'_H \times C_{H_2O} \quad (37').$$

[1] As the amount of salt formed is exceedingly small, hydrolysis being practically complete for such exceedingly weak bases, the concentration of the nonionized ester, C_{ester}, would not be measurably changed. It should be recalled that Walden (Ber. d. chem. Ges., **34**, 4185 (1901)) and Walker (*Ibid.*, **34**, 4115 (1901)) found that the oxonium bases are extremely weak. For instance, the affinity constant for dimethylpyrone is about 3×10^{-14}. Dimethylpyrone being one of the most pronounced bases among the oxonium bases the affinity constant for esters undoubtedly must be much smaller.

By comparison with the velocity equation (34′) for the decomposition of the acetate in the presence of water alone, equation (37′) shows us that the velocity is affected by the addition of the acid only by the increased concentration of the hydrogen ions (from C_H to C'_H) and proportionately to this change, which is in accord with the experimental facts.

We must now consider the well-known fact that the decomposition of methyl acetate by water is a reversible reaction, acetic acid and methyl alcohol giving methyl acetate and water, according to

$$CH_3COOH + CH_3OH \rightleftharpoons CH_3COOCH_3 + H_2O \quad (38)$$

and the fact that the velocity of this reaction is also accelerated by the addition of hydrochloric acid. Following out our conception rigorously, that hydrochloric acid acts only through salt, and subsequent ion, formation, we must conclude that this increased velocity must be due to weak basic properties of the acetic acid or the methyl alcohol and to consequent salt formation and ionization through the agency of the hydrochloric acid. Although methyl alcohol undoubtedly also has the power to form oxonium salts with acids,[1] the formation of methyl acetate must be due primarily to the minimal basic properties of acetic acid.[2]

It is no novel conception to find a compound exhibiting the amphoteric character of base and acid[3] and especially in the

[1] Baeyer: *Loc. cit.*

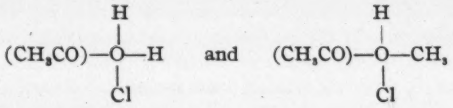
[2] If it were due to the basic properties of methyl alcohol and the primary formation of an acetate of methyl alcohol, the velocity of the formation of the ester would depend on the presence of the *nonionized* acetate,

$$CH_3COO.\overset{\overset{CH_3}{|}}{\underset{\underset{H}{|}}{O}}.H \rightleftharpoons CH_3COOCH_3 + H_2O \quad (39).$$

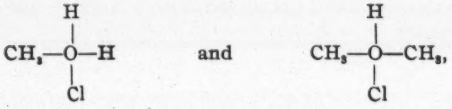
It is not conceivable that the *separate* ions of this salt, $CH_3\overset{\overset{+}{|}}{\underset{\underset{H}{|}}{O}}H$ and CH_3COO^-, could break down into methyl acetate, since each ion contains either no methyl or no acetate group and jointly they would give again the nonionized salt of equation (39). But there must be more nonionized acetate formed in the absence of a stronger acid, like hydrochloric acid, than in its presence; hence, the latter would have to retard, rather than accelerate, the esterification, if this depended on the basic functions of methyl alcohol.

[3] There are excellent reasons, in fact, for considering that all hydroxides known, even our strongest acids, like HNO_3, H_2SO_4, $HMnO_4$, are amphoteric and that some of their most important properties, for instance, their oxidizing power, are due to their *basic* ionization. See Stieglitz: "Qualitative Analysis," University of Chicago, 1905, p. 55.

case of so weak an acid as acetic acid. It is clear, too, that the salts

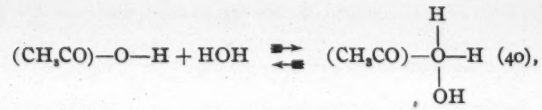


are entirely analogous to



the oxonium salts of methyl alcohol and methyl ether, the latter being the first oxonium salt known.[1] In experimental support of the basic functions of acetic acid, Rosenheim[2] found that acetic and other organic acids must form oxonium salts, for there is a perfect parallelism in their behavior and that of their esters towards chlorides, like antimony pentachloride. Euler[3] also arrived at the conclusion that the esterification of acetic acid must be due primarily to basic properties of acetic acid.

Applying rigorously then to esterification our fundamental conception that the accelerating action of hydrochloric acid must be due to the formation of a salt with a basic oxide, and finding that in the present case it must be the acetic acid that acts as a base, we have for acetic acid, forming an oxonium base with water,



(40),

and

$$C_{ac.\ acid} \times C_H \times C_{OH} = k'_1 \times C_{ac.\ base} \qquad (41);$$

[1] Friedel: Bull. Soc. Chim., **24**, 160 (1875).
[2] Ber. d. chem. Ges., **34**, 3377 (1901); **35**, 1115 (1902).
[3] Z. physik. Chem., **38**, 641 (1901).

and also

$$(CH_3CO)-\underset{\displaystyle OH}{\overset{\displaystyle H}{\underset{|}{\overset{|}{O}}}}-H \rightleftharpoons (CH_3CO)-\overset{+}{\underset{H}{O}}-H + \bar{O}H \quad (42),$$

giving

$$C_{ac.\,pos.\,ion} \times C_{OH} = k'_{base} \times C_{ac.\,base} \quad (43).$$

Dividing equation (43) by (41), we have

$$C_{ac.\,pos.\,ion} = \frac{k'_{base}}{k'_1} \times C_{ac.\,acid} \times C_H \quad (44).$$

If, in the esterification of acetic acid by methyl alcohol, as found for the imidoesters,[1] it is only the positive acet ion which reacts with the methyl alcohol, then we have for the velocity of esterification, according to equation (38),

$$\frac{dx}{dt} = k_e \times C_{ac.\,pos.\,ion} \times C_H \times C_{OCH_3} \quad (45).$$

For methyl alcohol we have

$$CH_3OH \rightleftharpoons \bar{C}H_3O + \overset{+}{H} \quad (46),$$

and

$$C_H \times C_{OCH_3} = k_{alc} \times C_{CH_3OH} \quad (47).$$

Introducing the values found in equations (44) and (47) into the velocity equation (45), we obtain for the speed of esterification in the absence of hydrochloric acid

$$\frac{dx}{dt} = k_e \times \frac{k_{base}}{k'_1} \times C_{ac.acid} \times C_H \times k_{alc} \times C_{CH_3OH} \quad (48),$$

$$= K_e \times C_{ac.\,acid} \times C_H \times C_{CH_3OH} \quad (48').$$

On adding hydrochloric acid to the system of acetic acid and methyl alcohol as given in equation (38), we would obtain a

[1] That the positive ions of the imidoesters form the "active mass" in other interactions than that with water is proved, as was anticipated, by the observations of Miss K. Blunt that, in the formation of *amidines* from imidoesters by the action of ammonia, the amidine formation is due to the action of ammonia on the positive imidoester ions, even though these are present only in *minimal*, but rigorously *calculable*, quantities. The results will be published in a later paper.

little of the hydrochloride of the oxonium base of acetic acid, the salt being largely hydrolyzed according to

$$(CH_3CO)\text{—}\underset{\displaystyle H}{\overset{\displaystyle Cl}{\underset{|}{\overset{|}{O}}}}\text{—}H + H_2O \rightleftharpoons (CH_3CO)\text{—}\underset{\displaystyle H}{\overset{\displaystyle OH}{\underset{|}{\overset{|}{O}}}}\text{—}H + HCl \quad (49).$$

According to equations (41) and (43), we must have for the free base in the hydrolyzed solution[1]

$$C_{ac.\,acid} \times C'_H \times C'_{OH} = k'_1 \times C'_{ac.\,base} \qquad (41'),$$

and

$$C'_{ac.\,pos.\,ion} \times C'_{OH} = k'_{base} \times C'_{ac.\,base} \qquad (43').$$

Dividing (43′) by (41′), we have

$$C'_{ac.\,pos.\,ion} = \frac{k'_{base}}{k_1} C_{ac.\,acid} \times C'_H \qquad (44').$$

Introducing the new concentration of the reacting positive ions of acetic acid into the velocity equation (45), we obtain, for the new condition,

$$\frac{dx}{dt} = k_e \times C'_{ac.\,pos.\,ions} \times C'_H \times C'_{OCH_3} \qquad (50),$$

$$= k_e \times \frac{k'_{base}}{k'_1} \times C_{ac.\,acid} \times C'_H \times k_{alc} \times C_{CH_3OH} \qquad (51),$$

$$= K_e \times C_{ac.\,acid} \times C'_H \times C_{CH_3OH} \qquad (51'),$$

as representing the velocity of esterification in the presence of hydrochloric acid.

By comparing equations (48′) and (51′), representing the velocities of esterification in the absence and the presence of hydrochloric acid, we learn from equation (51′) that the velocity is affected by the addition of the acid only by the increased concentration of the hydrogen ions (from C_H to C_H) and proportionately to this change. This conclusion, based on the theoretical development of the esterification catalysis as one

[1] $C_{ac.\,acid}$ is not *measurably* changed, as explained in footnote, p. 50. The same is true for C_{CH_3OH} in equation (47).

of salt and ion formation, is in agreement with the well-known experimental facts.

The condition for equilibrium in the reversible process of saponification and esterification,

$$CH_3COOCH_3 + H_2O \rightleftarrows CH_3COOH + CH_3OH \quad (31 \text{ and } 38),$$

is that the velocity of saponification should equal the velocity of esterification, and in the absence of hydrochloric acid we have, according to (34′) and (48′),

$$K_s \times C_{ester} \times C_{HOH} \times C_H = K_e \times C_{ac.\ acid} \times C_H \times C_{CH_3OH} \quad (52).$$

In the presence of hydrochloric acid, the condition of equilibrium follows from equating the expressions in (37′) and (51′):

$$K_s \times C_{ester} \times C_{HOH} \times C'_H = K_e \times C_{ac.\ acid} \times C'_H \times C_{CH_3OH} \quad (53).$$

The addition of hydrochloric acid would therefore, through salt and ion formation, accelerate the reactions in the reversed directions in the same proportions, and therefore it would not affect the final condition of equilibrium measurably; from both equations we get, by canceling the concentration of the hydrogen ions on both sides of each equation, the same expression for the condition of equilibrium,

$$K_s \times C_{ester} \times C_{HOH} = K_e \times C_{ac.\ acid} \times C_{CH_3OH} \quad (54),$$

which agrees with the results of experiment.

It is plain, from the above equations, that we may substitute any acid whatever for hydrochloric acid; its action would be strictly proportionate to the concentration of its hydrogen ions. The equations also bring out clearly the fact that the slow saponifying power of water itself is proportionate to its small concentration of hydrogen ions and that it is a catalyzer just to this extent.

[1] See Euler (Z. physik. Chem., **36**, 641 (1901), who pointed out that a catalyzer does not accelerate a reaction which would go of itself, but that the catalyzer is necessary also to allow the reaction to start and proceed at all.

It is clear, then, that the explanation that an acid accelerates an action simply through salt and ion formation, as was proved experimentally for imidoesters, may be extended to the catalysis of the acid esters, and, without a single new assumption, by the application of the ordinary laws of equilibrium it is found to be in perfect harmony with the three characteristic features of this catalysis: (1) the acceleration is proportionate to the concentration of the hydrogen ions present; (2) the acid does not appear to combine with any of the substances involved in the reaction; and (3) the ultimate condition of equilibrium is not measurably modified in the system. The acid does not *appear* to combine with the ester or the organic acid, simply because the salts are almost completely hydrolyzed under the conditions of the experiment and only very small quantities of the salts and their positive ions exist at any moment, owing to the extremely small affinity constants of the oxonium bases. But still the concentration of the active substance, the positive ion, would always remain proportionate to the concentration of hydrogen ions and the speed of change be proportionately accelerated, no matter how small the order of the actual concentration of the positive ions.

It must be added that unless the concentration of the salt and the positive ions at any moment were exceedingly small the final condition of equilibrium between ester, water, organic acid, and alcohol must be measurably affected by the addition of an acid, since the concentrations of the ester and of the organic acid would be decreased in somewhat different degrees if there were appreciable salt-formation.[1] The second and third characteristics of the catalysis of methyl acetate are therefore indissolubly connected. This would follow, of course, also from the consideration of the energy changes involved in these conditions. *They can be characteristic, consequently, only of such catalytic actions by acids (and bases) in which salts are formed to an extent beyond our methods of measurement, and they are never rigorously true.*

The first characteristic that the acceleration must be proportionate to the concentration of the catalytic agent likewise

[1] Footnotes, pp. 50 and 54.

can only be true for the limiting case of a practically complete hydrolysis, as is seen from the fundamental hydrolysis equation (6) and as is borne out by the behavior of the imidoesters.

The only fundamental property, consequently, which is necessarily common to all catalytic action by chemical reagents such as acids and which is really characteristic of catalysis is an ACCELERATION,[1] in a positive or negative sense, and this acceleration is due and proportionate to salt and ion formation. A perfectly similar conception applies, of course, to the action of alkalis and other chemical catalyzers, and unquestionably will apply to all kinds of catalyzers in the sense that they simply increase the concentration or active mass of a reacting component. The three other characteristics discussed above should then be considered incidental only to special, although important, conditions, in which the main feature, the acceleration, is produced by exactly the same change, salt and ion formation, but in which the imperfections of our methods of measurement still conceal the minimal but important changes in composition and equilibrium produced by the catalyzer.

It may be pointed out, here, that this explanation of catalytic action as due to the formation of salts and ions of greater or less stability or reactivity than the free bases or acids makes these actions, taken from the field of organic chemistry, appear simply as instances of well-known changes found in the realm of inorganic chemistry, where changes of reactivity and stability through salt formation and ionization are numberless; hydrochloric acid, added to ammonia, retards enormously the production and loss of ammonia, accelerates all actions in which ammonium ions are involved; potassium hydroxide retards the loss of carbonic acid from aqueous solutions, facilitates the production of carbonates. These are rough illustrations of the fact that salt formation changes the speed of reactions most decidedly. *Only when the salt formation is not obvious are we accustomed to speak of the change as proceeding "catalytically."*

[1] Page 30; *vide* also Vol. IV., Report of the Congress of Arts and Science, p. 278.

IV. The Mechanism of the Catalysis of Imidoesters and of Esters by Aqueous Acids.

Having established the fact that the accelerating action of hydrochloric acid in the decomposition of the imidoesters by water is directly proportionate to the positive ions formed with the imidoester, and that the conception of salt formation between hydrochloric acid and ordinary esters and organic acids, the last two acting as oxonium bases, is also in complete accord with the fundamental facts and gives us a rational theory for their catalysis, we may well ask how such changes in velocity of reactions must be considered from the point of view of the molecular structure of the compounds under discussion. The imidoesters will be considered first.

The decomposition of methyl imidobenzoate which is accelerated by hydrochloric acid is the following:

$$C_6H_5C(:\overset{+}{N}H_2)OCH_3 + HOH \rightarrow C_6H_5COOCH_3 + \overset{+}{N}H_4 \quad (2').$$

The water must act through its active constituents, the hydrogen and hydroxyl ions, and these will add to the double bond between the carbon and nitrogen atoms, as in many well-proved organic reactions,

$$C_6H_5C(:\overset{+}{N}H_2)OCH_3 + \overset{+}{H} + \overset{-}{OH} \rightarrow C_6H_5C(\overset{\overset{+}{N}H_3}{OH})OCH_3 \quad (55).$$

It must be the product of this action, the addition product formed, which ultimately suffers the decomposition in question,

$$C_6H_5C(\overset{\overset{+}{N}H_3}{OH})OCH_3 \rightarrow C_6H_5COOCH_3 + \overset{+}{N}H_4 \quad (56).$$

By considering (55) and (56) we find that hydrochloric acid would increase the concentration of the positive ion in both equations, and that its accelerating action may ultimately be due, then, to either or both of these causes: to the reactivity or additive power towards water of the positive ion $C_6H_5C(:\overset{+}{N}H_2)OCH_3$,

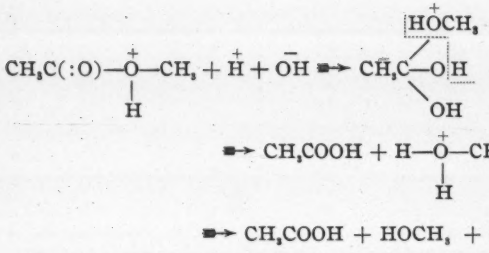
whose mass is increased (55); or to the instability, as given in (56), of the ion addition product $C_6H_5C(\overset{+}{N}H_3)(OH)OCH_3$, whose mass is also increased. It is, as yet, impossible to distinguish experimentally between these two possibilities, but on the basis of what follows we consider that it is most likely the instability of the addition product which is the ultimate cause of the action and of the accelerating effect of the hydrochloric acid.

It is characteristic that the result is the acceleration of a reaction according to which from one positive ion (the imidoester ion) is formed the positive ion (NH_4) of another base, ammonium hydroxide, which is much *stronger* than the original base, the imidoester. By comparing the reaction velocities and the affinity constants of analogous imidoesters, we have found, in fact, that the reaction velocities for closely related bases are greatest for the weakest bases.[1]

For instance, methyl imido-*m*-nitrobenzoate is a much weaker base than methyl imidobenzoate and its salt is decomposed very much faster than that of the latter. It will be observed that the weaker and less stable base is derived from the stronger acid, a fact which is of interest in connection with a similar observation by Euler[2] that the esters of the stronger acids are decomposed more rapidly by water than are those of the weaker acids. Here again we have a perfect parallelism between the imidoesters and the ordinary esters, only in the case of the former we have been able to obtain all the essential factors by experimental measurements.

If we apply the conclusions as to the mechanism of the decomposition of the imidoesters by water to the problems of esterification and saponification, we obtain the following as representing the course of the reactions, referred to the structures of the active substances. Since, as was shown in Part IV., the decomposition of an ester by water in the presence of an acid is due to the action of the active constituents of water on the positive oxonium ion of the ester, we have

[1] Full details on this point are contained in the article by Dr. McCracken.
[2] *Loc. cit.*

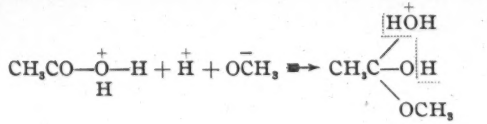


(57),

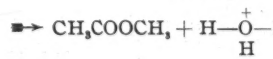
(58),

(59).

Again we note the tendency of one positive ion, the ester oxonium ion, to lose the positive ion of an undoubtedly stronger base, the oxonium ion of methyl alcohol; and *the same is true for the reversed reaction*, that of esterification, for which we have



(60),



(61),

(62).

The oxonium ion of water, H_3O, is formed first and there can be no question, although we are dealing with minimally small constants,[1] that water must form a much stronger oxonium base than does acetic acid.

It appears, then, that in the presence of acids there is a general tendency toward the formation of the positive ions of the strongest bases[2]—representing, most likely, the greatest de-

[1] The experimental determination of these and similar minimally small constants in organic chemistry undoubtedly will clear up most of the mysteries connected with organic reactions, just as the minute but exact constants for the instability of the complex ions, as determined by Bodlaender, Euler, and others, and the immense range of the constants of solution tensions have thrown wonderful light on many complex inorganic reactions which now appear as simple results of the fulfillment of definite, although often inconceivably large or minute, natural constants.

[2] In the presence of alkalis, we have, *vice versa*, a universal tendency towards the formation of strongest acids, *i. e.*, towards neutralization.

crease of free energy in a given system. This conclusion has found a further confirmation in our most recent observations on the action of ammonia on imidoesters; the action proceeds quantitatively according to

$$RC(:\overset{+}{N}H_2)OR' + NH_3 \rightarrow RC(:\overset{+}{N}H_2)NH_2 + HOR' \quad (63),$$

amidine ions being formed in a reaction with a very large velocity constant, rather than ammonium ions and an acid ester; of all the bases whose salts could be formed, the amidines are strongest.[1]

On the other hand, salts of the isoureas, which belong to the class of imidoesters, are remarkably stable toward water; they are not decomposed, even by hot water, into ammonium ions and ester; the action

$$NH_2C(:\overset{+}{N}H_2)OR + HOH \rightarrow NH_2COOR + \overset{+}{N}H_4 \quad (64)$$

does not take place,[2] as is the case for all other imidoesters. In this case where the decomposition does not take place, we have the significant fact that the affinity constant of the original base,[3] the isoureaester, is 6.4×10^{-5}, which is larger than that of ammonium hydroxide (1.8×10^{-5}), the base whose ion, NH_4, would be formed by a hydrolytic decomposition.[4]

V. Summary.

The results reported in this paper may be summarized as follows: (1) The catalytic action of acids has been proved to be due to the production of salts whose ions form the active mass in the reactions accelerated by acids. This has been proved quantitatively by measurements made with a large number of imidoesters. It has been confirmed by quantitative studies of the action of ammonia on imidoesters, the velocity of this action being proportionate to the concentration of the positive imidoester ion, although the latter forms a component only

[1] Miss Blunt will report in detail on this work, a preliminary report of which was read in December, 1906, at the meeting of the American Chemical Society.

[2] Stieglitz and McKee: THIS JOURNAL, **26**, 209 (1901).

[3] Bruce: J. Am. Chem. Soc., **26**, 419 (1904).

[4] In a later paper this question will be treated more fully on the basis of our most recent results, which, it may be said, agree perfectly with the above principle.

to an extent which is minute but rigorously calculable. When the action is retarded by the presence of an acid, the reacting component is the free, molecular base, and the retardation (negative acceleration) is again simply due to salt and ion formation.

(2) The rigorous application of the above principle to the catalysis of esters and to the process of esterification leads, with the aid of the laws of equilibrium and without any further assumptions, directly to all the fundamental equations expressing the course of such a catalysis or esterification, as well as to the fundamental equation expressing the condition of equilibrium arrived at in the reversible process.

(3) The same conception applied to catalytic actions by alkalis leads to the principle that their effect is due to the formation of salts whose negative ions form the active mass in the action.

(4) In reactions which are accelerated in acid solution there is the tendency to form positive ions of a base stronger than the original base undergoing decomposition.

(5) In accordance with the results, our views concerning catalytic action[1] must be modified in regard to all three of the commonly assumed fundamental characteristics of catalytic action, *viz.*, (1) that the acceleration must be proportionate to the concentration of the catalytic agent present; (2) that the agent must not appear to combine with any of the substances undergoing change; and (3) that the ultimate condition of equilibrium must not be measurably modified by the presence of a catalyzer. These characteristics are practically true only for limiting cases where the amount of salt formation is so small as to be beyond

[1] Reference should be made to Euler's papers on catalytic action, Z. physik. Chem., **36**, 641 (1901), and **47**, 353 (1904), in which the acceleration in the catalysis of methyl acetate, etc., is also explained on the basis of an assumed ionization of the organic compounds. How little the mere idea of ionization without the safe basis of experimental confirmation and measurements and without the application of the experience of organic chemistry can be relied upon to develop the subject from a purely mathematical standpoint is evident from the impossible reactions and forms of ionization of organic compounds which are assumed in a number of cases in the first, main paper. In the second, brief paper on the inversion of cane sugar, salt formation (as a carbonium salt) and hydrolysis is assumed somewhat as in this paper, but without experimental confirmation. It may be said that the work published here was already completed at the time this second paper of Euler's appeared and was reported during the same summer at the St. Louis Congress of Arts and Science (see page 29).

the scope of our measurements. None of them is absolutely true under any conditions. When the amount of salt formation becomes measurable, as for imidoesters, they need not hold even approximately, and *still the fundamental mechanism and mode of the catalysis is the same in these cases* as in the others. The one vital fact, then, of an acceleration due to an increase in the active mass or concentration of a reacting component in a catalytic action is the only fundamental fact common to all catalytic actions. Only for a special, but important and interesting, class of actions, the above principles hold as a very close approximation which can be derived, by the ordinary laws of chemical equilibrium, as a mathematical necessity from the fundamental principle laid down.[1]

Work is being continued along all of the above lines and will include also the study of the formation of acid amides by the action of ammonia on acid esters; the measurement, quantitatively, of the combination of acids with ordinary esters in their catalysis; and the quantitative effect of an added acid in the condition of equilibrium between acid, alcohol, ester, and water; the reactions of the acid nitriles in the presence of acids; and the study of the "Beckmann rearrangement" as an ionic reaction.

This statement has become necessary in consequence of an invasion of our field of work by another investigator.

ON PHENYLMALONIC NITRILE.

[SECOND PAPER.]

BY JOHN C. HESSLER.

In a preliminary paper,[2] the writer described the preparation of phenylmalonic nitrile and the attempt to prepare its

[1] The following studies on catalysis will shortly be published from this laboratory, the experimental work having already been completed:
Catalytic Reactions with Imidoesters, by J. Stieglitz.
The Catalysis of Imidoesters by Acids, by Ira H. Derby.
The Catalysis of Imidoesters, by Wm. McCracken.
The Catalysis of Imidoesters, by Hermann Schlesinger.
The Catalysis of Imidoesters as Affected by the Presence of Nonelectrolytes and Electrolytes, by Edith E. Barnard.
The Formation of Amidines, by Katharine Blunt.
The Action of Ammonia on Isoureaesters, by Robert A. Hall.
The Rearrangement of *o*-Aminophenylesters, by Louis A. Test.

[2] THIS JOURNAL, **32**, 119.

silver salt. This salt could not be isolated because of its instability, but there was obtained from it a substance, melting at 147° to 148°, which was analyzed. This substance turns out to be only one of several products formed by the spontaneous decomposition of the silver salt; a further study of these products is contained in the present paper. There is added, also, a description of several new derivatives of phenylcyanacetic ether and of phenylmalonic nitrile.

Silver Salt of Phenylmalonic Nitrile.

Twenty grams of phenylmalonic nitrile were converted, as previously described,[1] into the silver salt. This was dried over night on a clay plate. A sample dried *in vacuo* over sulphuric acid and then ignited gave 44.27 per cent of silver. Calculated for $C_9H_5N_2Ag$, 43.37 per cent. The remainder of the salt was extracted eight times with boiling ether. The organic material extracted by the ether was left, after the solvent had been distilled, as a pasty, white mass. The insoluble residue weighed 17.2 grams when dried on a clay plate.

When the organic material extracted by ether was treated again with cold ether, all except a small amount (0.2 to 0.3 gram) dissolved. This insoluble portion was filtered off and dried on a clay plate; it melted with decomposition at 210° to 215°.

The ether filtrate was concentrated to 250 cc., an equal volume of ligroin (boiling at 40° to 60°) was added, and the mixture was left in a room at winter temperature for two days. There was obtained a white, pasty precipitate which weighed about 3 grams. It was filtered off, and the ether-ligroin solution was then concentrated to 250 cc. and allowed to cool. An almost colorless oil separated out; after some hours this solidified to almost colorless crystals which melted at 87° to 88° after being dried on a clay plate. By successive concentrations of the ether-ligroin mother liquor and by addition of some of the crystals first obtained to the oil which separated out, there were collected in all 7.7 grams of the solid melting at 87° to 88°.

[1] THIS JOURNAL, **33**, 125.

The pasty precipitate mentioned above (weight, about 3 grams) was treated with ether; only 0.35 gram remained insoluble; this melted at 210° to 220° with decomposition. The ether filtrate was treated with ligroin (40° to 60°) and gave 0.9 gram of the apparently amorphous powder melting at 147° to 148°. The filtrate from this, after being concentrated, gave a further small amount of the crystals melting at 87° to 88°.

It is evident, therefore, that at least *three* organic substances result when the silver salt of phenylmalonic nitrile is decomposed; these melt at 87° to 88°, at 147° to 148°, and at approximately 210° to 220°, respectively.

Dimolecular Phenylmalonic Nitrile.

A. *Analysis.*—The body melting at 87° to 88° was recrystallized from ether-ligroin and dried *in vacuo* over sulphuric acid.

I. 0.2057 gram substance gave 0.5707 gram CO_2 and 0.0689 gram H_2O.

II. 0.1502 gram substance gave 0.42 gram CO_2 and 0.0552 gram H_2O.

III. 0.1272 gram substance gave 22.3 cc. N at 20° C. and 747 mm.

	Calculated for $(C_9H_6N_2)_2$.	Found. I.	II.	III.
C	76.06	75.67	76.26	. .
H	4.22	3.72	4.08	. .
N	19.72	. .	. .	19.8

The substance is burned with great difficulty. In combustion II. it was mixed with cupric oxide in wire form; in the others, powdered cupric oxide was used. The last portions of nitrogen came off only at bright red heat.

B. *Molecular Weight.*—Molecular weight determinations of the body melting at 87° to 88°, made by the boiling point method, agree fairly well with the dimolecular formula $(C_9H_6N_2)_2$. The apparatus was that of McCoy;[1] the solvents used were benzene and absolute alcohol.

a. In Benzene Solution (constant = 3280).—1.0171 grams substance caused a rise of 0.31° C. in the boiling point of the

[1] This Journal, **23**, 353–360.

solution when its volume was 32.5 cc., and of 0.303° C. when the volume was 34.8 cc.

	Calculated for $(C_9H_6N_2)_2$.	Found. I.	II.
Mol. wt.	284	331	316

b. In Alcoholic Solution (constant = 1560).—1.3372 grams substance caused a rise of 0.203° C. when the volume of the solution was 33.6 cc., and of 0.188° when the volume was 35.2 cc.

	Calculated for $(C_9H_6N_2)_2$.	Found. I.	II.
Mol. wt.	284	306	315

C. *Properties.*—Dimolecular phenylmalonic nitrile dissolves readily in alcohol and ether. Water precipitates it from alcoholic solution as an oily liquid which soon crystallizes in hard granules melting at 87° to 88°. From benzene solution the substance did not crystallize readily. The solution was therefore treated with an equal volume of ligroin (40° to 60°) and allowed to stand overnight. The substance then crystallized in large, white plates which melted at 67° to 68° after they had been dried for five minutes on a clay plate. When the crystals were left in the air they shrank together and became very sticky; at the same time benzene was given off. A determination of the combined benzene gave the following result:

1.0202 grams substance (dried five minutes on a clay plate) were left *in vacuo* over sulphuric acid until no further loss of weight took place (50 days). The total loss of benzene was 0.2164 gram.

	Calculated for $(C_9H_6N_2)_2.C_6H_6$.	Found.
C_6H_6	21.55	21.21

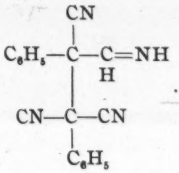
The residue of dimolecular phenylmalonic nitrile melted sharply at 87° to 88°. Heated on a nickel spatula the substance is decomposed, giving off pungent, red vapors. It dissolves readily in caustic soda solution to form the sodium salt. The amount of alkali required indicates that the dimolecular nitrile is monobasic; one gram of it was just dissolved by 3.5 cc. of normal sodium hydroxide solution.

An absolute ether solution of the nitrile was treated with sodium in the form of chips. After two weeks the sodium

had been converted into the yellow sodium salt; this was insoluble in ether but readily soluble in water.

The solution obtained from the nitrile and the theoretical amount of normal sodium hydroxide gave, when poured into silver nitrate solution, a white precipitate of the silver salt (*q. v.*).

A possible formula for the dimolecular nitrile, based upon its known properties, is this:



The hydrogen of the imine group would thus be the ionic hydrogen.

Trimolecular Phenylmalonic Nitrile.

The analysis of the substance melting at 147° to 148° was reported in the preliminary paper (*q. v.*). A molecular weight determination by the method of McCoy gave results indicating that the substance is probably trimolecular phenylmalonic nitrile.

0.7599 gram substance, in benzene solution, caused a rise of 0.165° C. in the boiling point when the volume of the solution was 32.6 cc.

Calculated for $(C_9H_6N_2)_3$.	Found.
426	463

Oxidation of Phenylmalonic Nitrile and Its Polymers by Means of Chromic Acid.

Phenylmalonic nitrile and both its polymers give *the same substance* when oxidized with chromic acid in glacial acetic acid solution. The product is an amorphous solid melting at 210° to 230° with decomposition, and gives, when analyzed, values agreeing with the formula $(C_9H_6N_2)_x$. On this account it seems probable that the oxidation of each $C_9H_6N_2$ molecule (or group) results in the loss of one atom of hydrogen. The be-

havior of the sodium salt of phenylmalonic nitrile with bromine (*q. v.*) makes this still more likely.

A. *Oxidation of Phenylmalonic Nitrile.*—Phenylmalonic nitrile (0.5 gram), specially purified by recrystallization from dilute alcohol, was dissolved in 10 cc. of glacial acetic acid and treated with chromic acid in the same solvent. The chromic acid solution was added drop by drop: the color of the first few drops was changed in a few seconds to bright green, and at the same time an amorphous, white solid was precipitated. Altogether, 0.5 gram of chromic acid was added. The amount theoretically necessary to give one atom of oxygen for every two molecules of the nitrile ($C_9H_6N_2$) is 0.12 gram. The mixture was allowed to stand overnight. Water was added to precipitate the oxidation product, which was filtered off, washed with water, and dried on a clay plate and *in vacuo* over sulphuric acid. The substance melted at 215° to 230° with decomposition.[1]

0.1426 gram substance gave 0.3997 gram CO_2 and 0.0492 gram H_2O.

	Calculated for $(C_9H_6N_2)_x$.	Found.
C	76.59	76.43
H	3.55	3.83

B. *Oxidation of Dimolecular Phenylmalonic Nitrile by Chromic Acid.*—Five-tenths of a gram of the dimolecular nitrile, $(C_9H_6N_2)_2$, was dissolved in glacial acetic acid and treated with an excess of chromic acid dissolved in the same solvent. As in the case of phenylmalonic nitrile, the chromic acid was reduced and a white solid was precipitated. The precipitate was washed with water and dried on a clay plate and *in vacuo* over sulphuric acid. It weighed 0.5 gram. When heated in a melting point tube at 215° to 230°, it is decomposed.

0.1573 gram gave 0.4418 gram CO_2 and 0.0532 gram H_2O.

	Calculated for $(C_9H_6N_2)_x$.	Found.
C	76.59	76.61
H	3.55	3.76

[1] A special experiment with benzylmalonic nitrile (THIS JOURNAL, **22**, 180) showed that this substance is not oxidized by chromic acid in glacial acetic acid solution.

C. *Oxidation of Trimolecular Phenylmalonic Nitrile.*—The trimolecular nitrile, melting point 147° to 148°, gave, when treated with chromic acid in acetic acid solution, an amorphous white solid having exactly the same properties as the substance obtained from phenylmalonic nitrile and from the dimolecular body.

It will be noticed that a small amount of a substance having approximately the same properties was obtained from the products formed by the decomposition of the silver salt of phenylmalonic nitrile. It was difficultly soluble in ether and melted with decomposition at 210° to 215°. This must have been formed by the oxidation of phenylmalonic nitrile or of its polymers by means of silver oxide.

Action of Sodium Phenylmalonic Nitrile with Bromine.—The sodium salt of phenylmalonic nitrile was subjected to the action of bromine in the expectation that phenylbrommalonic nitrile would be produced, but the chief product seems to be the amorphous solid melting with decomposition at 215° to 230° which was produced by the oxidation with chromic acid.

A. *Addition of Bromine to the Sodium Salt.*—To 3 grams of sodium phenylmalonic nitrile, suspended in 30 cc. of chloroform, there was added, drop by drop, a solution of bromine in chloroform. One atomic weight of bromine was used for every molecular weight of the sodium salt. A white precipitate of sodium bromide separated out. It was filtered off, dried, and weighed. 1.5 grams were obtained instead of 1.9 grams, the theoretical amount. The chloroform solution, when distilled on a water bath, left an oily liquid which was difficultly soluble in ether. It was redissolved in chloroform and precipitated by ligroin; 0.9 gram of an amorphous, white solid was obtained. A second reprecipitation from chloroform solution by means of ligroin yielded 0.45 gram of the substance. It shrank together at 210° to 220° and melted to a black tar at 230°. It was dried *in vacuo* over sulphuric acid and analyzed.

I. 0.1473 gram substance gave 0.4097 gram CO_2 and 0.0489 gram H_2O.

II. 0.1153 gram substance gave 19.8 cc. N at 19.5° C. and 742.8 mm.

	Calculated for $(C_9H_5N_3)_x$.	Found.
C	76.59	75.86
H	3.55	3.69
N	19.86	19.32

The substance is burned with difficulty. Possibly it contains a trace of bromine. Its formation probably takes place according to the equation

$$xC_9H_5N_2Na + xBr \rightarrow (C_9H_5N_3)_x + xNaBr.$$

B. *Addition of Sodium Phenylmalonic Nitrile to Bromine* (two atoms).—Two and eight-tenths grams of sodium phenylmalonic nitrile were added in portions of 0.1 gram each to a solution of 3 grams of bromine in 40 cc. of chloroform. The temperature rose to 35°, a large excess of bromine remained, and a white precipitate of sodium bromide appeared. The mixture was treated with water in a separatory funnel and the chloroform solution was dried with calcium chloride and then distilled. When about four-fifths of the chloroform and the excess of bromine had been removed, a white, crystalline solid separated out. This was filtered off and found to weigh 0.35 gram. It melted at 117°. The substance is soluble in chloroform, difficultly soluble in alcohol, and insoluble in ligroin (40° to 60°). It crystallized from benzene in small granules melting at 118°. The substance was at first supposed to be phenylbrommalonic nitrile but it was later shown that no bromine was present.

0.1051 gram substance gave 0.2958 gram CO_2 and 0.0399 gram H_2O.

	Calculated for $(C_9H_6N_2)_x$.	$(C_9H_5N_3)_x$.	Found.
C	76.06	76.59	76.75
H	4.22	3.55	4.21

The small amount of the substance available has prevented its further investigation up to the present time. The filtrate from the crystals melting at 117° gave gummy substances when concentrated; there was also obtained 0.15 gram of the amorphous solid melting with decomposition at 215° to 230°.

C. *Addition of Sodium Phenylmalonic Nitrile to Bromine* (one atom).—Three and eight-tenths grams of sodium phenyl-

malonic nitrile were added in 0.2 gram portions to a solution of 1.9 grams (one atom) of bromine in 50 cc. of chloroform. All the bromine reacted. The sodium bromide was filtered off and the filtrate was distilled. Not a trace of the solid melting at 117° was obtained, but only a thick gum which gave, when treated with ether, 1.7 grams of the white solid melting at 210° to 230°. A repetition of this experiment with a slight excess of bromine gave only traces of the solid melting at 117°; the chief product is the amorphous substance decomposing at 210° to 230°.

The Silver Salt of Dimolecular Phenylmalonic Nitrile.

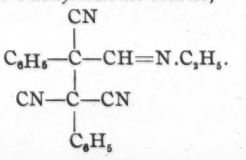
It has already been stated that when the sodium salt of dimolecular phenylmalonic nitrile is added to a solution of silver nitrate the silver salt is precipitated. One gram of the nitrile was dissolved in the theoretical amount, 3.5 cc., of normal sodium hydroxide solution and the resulting solution of the sodium salt added to an excess of silver nitrate solution. The precipitate was almost pure white and did not become dark when filtered. It changed color, however, when dried on a clay plate. It was dried *in vacuo* over sulphuric acid until its weight was constant. The amount obtained was considerably over one gram.

0.2433 gram substance gave, on ignition, 0.0669 gram Ag.

	Calculated for $C_{18}H_{11}N_4Ag$.	Found.
Ag	27.62	27.49

The dark colored silver salt was extracted with ether, but only a trace went into solution; the salt is not, therefore, decomposed appreciably at the ordinary temperature. It is decomposed, however, when heated on a water bath at 90°.

Ethyl Dimolecular Phenylmalonic Nitrile,



—When one gram of the silver salt of dimolecular phenylmalonic nitrile was added to 4 grams of ethyl iodide (theory, 1.56 grams), the two substances reacted with a hissing noise and the mixture became decidedly warm. After standing one hour the mixture was heated to 80°, cooled, and filtered. The silver iodide weighed 0.5 gram. The filtrate was distilled *in vacuo* and 0.6 gram (theory, 0.8 gram) of a slightly colored, gummy residue was obtained. This was dissolved in ether and the solution was treated with ligroin (40° to 60°). After two days there was obtained a crop of crystalline plates grouped in rosettes. These melted at 101° to 102° after being dried *in vacuo* over sulphuric acid.

0.1442 gram substance gave 22.8 cc. N at 22° C. and 744.5 mm.

	Calculated for $C_{20}H_{16}N_4$.	Found.
N	17.95	17.63

n-Butyl Dimolecular Phenylmalonic Nitrile,

$$C_9H_8N_2.C_9H_5N_2.C_4H_9.$$

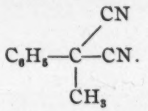
—One and a half grams of the silver salt were added to 7.5 grams of *n*-butyl iodide. As with ethyl iodide, the temperature rose to 40°. The mixture was allowed to stand a week; a faint odor of isocyanide was noticed. Ether was then added, the silver iodide filtered off, and the filtrate distilled up to 70° *in vacuo* (20 mm.). The residue was a slightly colored, thick gum and weighed 1.25 grams, practically the theoretical amount. The gum was dissolved in ether, treated with ligroin (40° to 60°) until the ether solution began to be turbid, and allowed to stand for a week in the cold. Large, crystalline plates were thus obtained which were aggregated in rosettes. The melting point of the crude substance was 79° to 80°. After the body had been washed with ether it was perfectly white and melted at 80° to 81°.

0.1548 gram gave 23.5 cc. N at 27° and 745.4 mm.

	Calculated for $C_{25}H_{20}N_4$.	Found.
N	16.47	16.54

Both the ethyl and the *n*-butyl bodies gave off their nitrogen very slowly; the last portions only at a bright red heat.

Methylphenylmalonic Nitrile,



—Three grams of sodium phenylmalonic nitrile were treated with 12 grams (the theoretical amount is 2.6 grams) of methyl iodide. Since there was no apparent action at the ordinary temperature the mixture was heated in a sealed tube for 9 hours. The product was treated with water and extracted with ether; the ether solution was then washed with 10 per cent sodium hydroxide solution, dried with calcium chloride, and distilled on a water bath. There remained an oily substance which was distilled at 125° to 130° under 16 mm. pressure. Yield, 1.8 grams.

I. 0.1708 gram substance gave 0.4797 gram CO_2 and 0.0837 gram H_2O.

II. 0.1178 gram substance gave 19.4 cc. N at 23° C. and 748.1 mm.

	Calculated for $C_{10}H_8N_2$.	Found. I.	II.
C	76.92	76.60	. .
H	5.13	5.44	. .
N	17.95	. .	18.36

Attempts to get the substance in solid form were not successful.

Action of Sodium Phenylmalonic Nitrile with Benzenediazonium Chloride.

Phenylmalonic nitrile (3.5 grams), dissolved in 20 cc. of absolute alcohol, was treated with 0.57 gram (one atomic equivalent) of sodium, and the resulting solution of the sodium salt was added in small portions to an ice-cold, aqueous solution containing one molecular equivalent of benzenediazonium chloride. The precipitate that separated out was oily at first, but it soon solidified and was almost white. The solution became red and then dark blue. The blue color persisted several

days. The substance which produced it could be extracted with ether; dilution with water caused it to disappear, while addition of absolute alcohol restored it. The resulting diazonium body was dried on a clay plate for 45 minutes. It weighed 4.2 grams. A portion that was left in a moist condition upon a funnel exploded. The dried substance was also decomposed with a slight explosion when warmed. When it was treated with ether, the substance gave off nitrogen.

Two grams of the dried diazonium body were added to 25 cc. of ether in a flask connected with an azotometer, the gas evolved being first passed through a wash bottle of alcohol. The theoretical amount of nitrogen capable of being produced from the benzenediazonium group is about 180 cc. under standard conditions; the amount actually collected was 82 cc., measured under ordinary conditions of temperature and pressure, but as the evolution of gas went on even in the absence of ether much nitrogen had undoubtedly been given off in the process of drying.

During the evolution of the nitrogen a white solid was precipitated; this weighed 0.2 gram after it had been dried on a clay plate, and melted at 107°. The ether solution gave, on evaporation, a thick, tarry liquid which solidified, in part, *in vacuo*. It has not been examined further.

An analysis of the solid melting at 107° showed that it was either another polymeric phenylmalonic nitrile or a substance of the formula $(C_9H_5N_2)_x$.

0.1396 gram substance gave 0.3928 gram CO_2 and 0.0505 gram H_2O.

	Calculated for $(C_9H_6N_2)_x$.	Calculated for $(C_9H_5N_2)_x$.	Found.
C	76.06	76.59	76.72
H	4.22	3.55	4.02

Action of Phenylcyanacetic Ether with Ammonium Hydroxide (repeated); *Phenylcyanacetamide.*

The preparation of phenylcyanacetamide, already described in the preliminary paper, has been repeated with the following results:

Forty grams of phenylcyanacetic ether, boiling at 160° to 170° under 18 mm. pressure, were treated with 70 grams of

concentrated, chemically pure ammonium hydroxide (sp. gr. 0.90). The ester dissolved at once. A large amount of the amide separated out in 15 minutes when the solution was treated with a crystal of the same substance. After 5 hours the crystals were filtered off and dried on a clay plate. They weighed 23.7 grams. Water was added to the ammoniacal filtrate and the diluted solution allowed to stand overnight. In this way 2.6 grams more of the amide were obtained, making a total of 26.3 grams, or 80 per cent of the theoretical amount.

When the ammoniacal solution was acidified with dilute sulphuric acid and extracted with ether, there were obtained 3.8 grams of phenylcyanacetic acid. When this was recrystallized from 12 grams of benzene, 2.7 grams were obtained, which melted at 93° to 94° after being dried over sulphuric acid *in vacuo*.

Twenty-seven grams of the amide gave, when crystallized from 150 cc. absolute alcohol, 21.6 grams of six-sided prisms.

Action of Phenylcyanacetic Ether with Aniline, with the Toluidines, and with Phenylhydrazine.

1. *Phenylcyanacetanilide.*—Two grams of the ester and 2 grams (twice the theoretical amount) of aniline were heated over a free flame until alcohol distilled off. The residue was a thick gum which solidified when cold. It was treated with ether, filtered off, and dried on a clay plate. There were obtained 1.9 grams of phenylcyanacetanilide. When crystallized from absolute alcohol, it separated out in grouped needles melting at 136°. The anilide is only slightly soluble in ether and practically insoluble in water. Analysis gave the following results:

I. 0.1562 gram substance gave 0.4358 gram CO_2 and 0.0739 gram H_2O.

II. 0.1848 gram substance gave 19.4 cc. N at 19° C. and 747.3 mm.

	Calculated for $C_{15}H_{12}ON_2$.	Found. I.	II.
C	76.27	76.09	. .
H	5.08	5.26	. .
N	11.87	. .	11.91

2. *Phenylcyanacetic Acid Toluidides.*—Phenylcyanacetic ether and *p*-toluidine were heated until no more ethyl alcohol distilled off. The residual liquid crystallized when cold. When recrystallized from absolute alcohol the *p*-toluidide separated out in long needles melting at 139°. The ortho- and meta-toluidides were made in the same way; the ortho body melted at 139° and the meta compound at 131°. All the toluidides are more easily soluble in ether than the anilide. All are difficultly soluble in water.

3. *Phenylcyanacetic Acid Phenylhydrazide.*—Three and three-tenths grams of the ester and 2 grams (the theoretical amount) of phenylhydrazine were heated to 150° to 200° in a metal bath until no more alcohol could be distilled off. The crude phenylhydrazide melted at 207°.

The same substance was formed when phenylcyanacetic ether was allowed to stand several days with an excess of phenylhydrazine.

The phenylhydrazide is soluble in about 30 parts of boiling absolute alcohol and crystallizes from the alcoholic solution in large, hard granules melting at 224°. It is difficultly soluble in ether and insoluble in water. It was recrystallized from alcohol for analysis.

0.1447 gram substance gave 22.5 cc. N at 26.5° C. and 743.8 mm.

	Calculated for $C_{15}H_{13}ON_3$.	Found.
N	16.73	16.94

Action of Sodium upon Carbonic Acid Ethyl Ester and Malonic Nitrile.

Two grams of sodium in wire form were added to 10 grams of carbonic ether and 5.6 grams of malonic nitrile, dissolved in 200 cc. of absolute ether. The reaction was a slow one, but after a week the sodium had disappeared. The sodium salt was filtered off and dried over sulphuric acid *in vacuo*. Yield, 7.5 grams. Analysis showed that the substance was sodium malonic nitrile.

0.4239 gram substance gave 0.3376 gram Na_2SO_4.

	Calculated for $CHNa(CN)_2$.	Found.
Na	26.13	25.76

Action of Hydrochloric Acid upon an Alcoholic Solution of Phenylmalonic Nitrile.

Two grams of phenylmalonic nitrile dissolved in 20 cc. of absolute alcohol were treated with 20 cc. concentrated, chemically pure hydrochloric acid of specific gravity 1.2. Ammonium chloride crystallized out in a few hours; after three days it was filtered off and the filtrate was distilled *in vacuo* up to 55°. The residue contained more ammonium chloride; this was removed by treatment with absolute alcohol. Altogether, 0.55 to 0.6 gram of ammonium chloride was obtained.

The absolute alcohol was then removed *in vacuo* and the residue was treated with water and extracted with ether. The ether solution was separated into (*a*) a portion soluble in 10 per cent sodium carbonate and (*b*) a portion neutral to sodium carbonate.

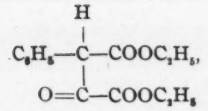
(*a*) The sodium carbonate solution was acidified with dilute sulphuric acid and extracted with ether, and the ether solution dried with calcium chloride. Distillation of the ether left about 0.2 gram of an oily liquid which solidified *in vacuo* over sulphuric acid. Its properties were those of phenylcyanacetic acid; it melted at 90° to 92° when crystallized from benzene and was decomposed at 140° to 165° with evolution of carbon dioxide.

(*b*) The ether solution containing the substances neutral to sodium carbonate was distilled on a water bath. There remained an oily liquid which consisted chiefly of phenylcyanacetic ether and phenylcyanacetamide. When it was treated with ether about 0.1 gram of the amide remained as white crystals melting at 147° to 148°. The ether solution gave 1.35 grams of pure phenylcyanacetic ether boiling at 161° to 162° under 16 mm. pressure. It was treated with concentrated ammonia water and thus converted into the pure amide melting at 149° to 150°.

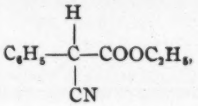
Phenylcyanpyroracemic Acid Ethyl Ester.

Since W. Wislicenus was able to prepare phenylmalonic ether by splitting off carbon monoxide from phenyloxalacetic ether,[1]

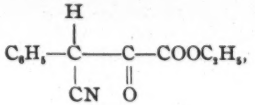
[1] Ber. d. chem. Ges., **20**, 593; **27**, 1091.



the writer hoped to be able to prepare *phenylcyanacetic ether*,



from *phenylcyanpyroracemic acid ethyl ester*,



by a similar reaction. The attempt was not successful, but the results of the experiments are given. Erlenmeyer, jun., prepared phenylcyanpyroracemic ether from benzyl cyanide, oxalic ether, and sodium.[1] His method was repeated, as follows:

Twenty-five grams of oxalic ether and 21 grams of benzyl cyanide (practically molecular quantities) were dissolved in 100 cc. of absolute ether and treated with 4 grams (one atomic equivalent) of sodium in wire form. The reaction was noticeable only after about one hour and was controlled by means of running water. After the sodium had disappeared the product of the reaction was allowed to stand for 24 hours. The sodium salt had then separated out. Water and dilute sulphuric acid were added and the solid ester, together with some unchanged benzyl cyanide and oxalic ether, was extracted with ether. Twenty-seven grams of the crude substance were obtained. It could be recrystallized from hot water and from ether-ligroin. When purified it melted at 129° to 130°. An analysis gave the following result:

[1] Ann. Chem. (Liebig), 271, 172.

0.2096 gram substance gave 0.5108 gram CO_2 and 0.0986 gram H_2O.

	Calculated for $C_{12}H_{11}O_2N$.	Found.
C	66.36	66.46
H	5.07	5.23

Phenylcyanpyroracemic acid ethyl ester is readily soluble in alcohol, chloroform, and ether. It is distilled without decomposition at 206° under 20 mm. pressure. Ten per cent caustic soda extracts it from ether solution. Concentrated ammonia water dissolves it, giving, after some hours, oxamide and benzyl cyanide in practically theoretical amounts. It is soluble, also, in aqueous sodium carbonate, and is precipitated from the solution by dilute sulphuric acid.

Effect of Heat upon Phenylcyanpyroracemic Acid Ethyl Ester.

Four and six-tenths grams of the ester were heated at 230° to 240° in a distilling flask connected with a receiver and an azotometer. The volume of gas collected was 300 cc. It burned like carbon monoxide, and the last 100 cc. were completely absorbed by ammoniacal cuprous chloride. On raising the temperature to 300°–350° about 2 cc. of a liquid distilled over into the receiver. This boiled at 100° to 140° at 15 mm.

A similar result was obtained when the ester was heated to 240°–250° under ordinary pressure until the carbon monoxide had been driven off and the residue was then heated *in vacuo* (15 mm.). The substance sought was not formed in appreciable quantity.

Decomposition of the Ester by Aqueous Sulphuric Acid.

An ether solution of the crude ester was shaken three times with 10 per cent sodium hydroxide solution; practically all the ester was thus removed from the ether. After 20 minutes the alkaline solution was treated with an excess of dilute sulphuric acid. At first a yellow precipitate was formed but this redissolved when the mixture was shaken. The solution then became turbid, owing to the separation of drops of an oily liquid. After 14 hours the liquid had solidified and carbon dioxide was being evolved. When the acid solution was heated on a boiling

water bath streams of carbon dioxide came off; this was completely soluble in 10 per cent sodium hydroxide. The hot solution was filtered and allowed to cool. It deposited about 4 grams of white crystals. These melted at 157° when dried on a clay plate and over concentrated sulphuric acid *in vacuo*. Analysis showed that the substance was phenylpyroracemic acid.[1]

0.1543 gram gave 0.3735 gram CO_2 and 0.0694 gram H_2O.

	Calculated for $C_9H_8O_3$.	Found.
C	65.85	66.01
H	4.88	4.99

The study of phenylmalonic nitrile and its derivatives is being continued.

UNIVERSITY OF CHICAGO,
Aug. 27, 1907.

Contributions from the Chemical Laboratory of Harvard College.

ON TRIBROMMETHOXYORTHOBENZOQUINONE-MONOMETHYLHEMIACETAL.

BY C. LORING JACKSON AND H. A. FLINT.

In continuing the work[2] on derivatives of tetrabromorthobenzoquinone, which has been carried on for some time in this laboratory, we have made good progress in the study of the oxidation product, $C_8Br_4O_2$, discovered by Russe and one of us,[3] but we have decided to postpone the publication of our results until its constitution is entirely settled, which we hope to accomplish early in the following year.

In the present paper, we describe the tribrommethoxyorthoquinonemonomethylhemiacetal, the work on which is finished. Perhaps the most striking difference between the behavior of tetrachlor- and tetrabromorthoquinone with methyl and other alcohols lay in the fact that with the chlorine compounds

[1] *Cf.* W. Wislicenus: Ber. d. chem. Ges., **20**, 592. Erlenmeyer, jun.: Ann. Chem. (Liebig), **271**, 174.

[2] Jackson and Porter: THIS JOURNAL, **30**, 518 (1903); **31**, 89 (1904). Jackson and Carlton; **34**, 422 (1905). Jackson and Shaffer, **34**, 460 (1905). Jackson and Russe: **35**, 154 (1905). Jackson and MacLaurin: **37**, 87 (1907).

[3] *Ibid.*, **35**, 183 (1905).

the halogen is easily replaced, whereas, according to all previous work, the reaction with the bromine compound is confined to the quinone oxygen atoms. Thus tetrachlororthoquinone gave the following products:[1] $C_6Cl_3OCH_3O(OCH_3OH)$, $C_6Cl_3OHO_2$, $C_4Cl_3(OH)_2O_2$, $C_6Cl_4O_2C_6Cl_2O(OCH_3OH)$, $C_6Cl_4O_2C_6Cl_2(OCH_3OH)_2$, and $C_6Cl_4OCH_3O_3HOC_6Cl_4$, the chlorine remaining unaffected only in the last. Tetrabromorthoquinone, under the same conditions, gave[2] $(C_6Br_4O_2)_4CH_3OH$ and $C_6Br_4OOCH_3OHOOC_6Br_4$, in neither of which is the halogen attacked. We have discovered now that, in making the α-compound (that last mentioned above) by the action of cold methyl alcohol on tetrabromorthoquinone, there is always formed, at the same time, a little of the tribrommethoxyorthoquinonemonomethylhemiacetal, $C_6Br_3OCH_3O(OCH_3OH)$, exactly analogous to the first body in the chlorine series,[3] which was overlooked before because it remained in solution in the methyl alcohol mother liquors. Its formation accounts for the small amount of hydrobromic acid so frequently observed during the preparation of the α compound. If the tetrabromorthoquinone is treated with hot, instead of cold, methyl alcohol, the tribromhemiacetal becomes the principal product, little, if any, of the α compound being formed. The previous statement that the halogen is not affected when the tetrabromorthoquinone is treated with methyl alcohol, therefore, is not true but must be changed to the following: tetrabromorthoquinone shows much less tendency than the tetrachlor compound to undergo attack on the halogen when treated with methyl alcohol, the reaction which affects the halogen remaining comparatively insignificant if the methyl alcohol acts in the cold, whereas with the tetrachlororthoquinone this is a principal reaction under these conditions.

The tribrommethoxyorthoquinonehemiacetal, $C_6Br_3OCH_3O(OCH_3OH)$, melts at 138°. This is strange, as the corresponding trichlor compound melts at 138°–140°. Its constitution was determined by convertin git into the acetyl compound, $C_6Br_3OCH_3O(OCH_3OC_2H_3O)$, which melts at 158° (the

[1] This Journal, **38**, 127 (1907).
[2] *Ibid.*, **31**, 95 (1904); **34**, 425 (1905).
[3] *Ibid.*, **38**, 142 (1907).

trichlor compound melts at 149°–150°). This proves that it contains one hydroxyl group. On treatment with phenylhydrazine, the acet compound was converted into the phenylhydrazone, $C_6Br_3OCH_3N_2HC_6H_5(OCH_3OC_2H_3O)$, melting at 205° (whereas the trichlor hydrazone melts at 235°), which proves the presence of the carbonyl group of the quinone. These two observations establish the fact that it is a monohemiacetal.

When heated with hydrobromic acid, it is converted into the oxyquinone, $C_6Br_3OHO_2$, red plates melting at 205°, which so closely resembles, in all its properties, the trichloroxyparaquinone melting at 198° that we feel convinced it is also a paraquinone, the purple solution formed from each compound with water or alcohol being particularly distinctive. On the other hand, the tribrom compound is decidedly redder than the chlorine body, but, as far as we can find, this deeper color might be produced by the presence of bromine, instead of chlorine, in the molecule, and, in any case, this difference is not sufficiently significant, in view of the many resemblances between the two bodies, to make it worth while to submit the constitution of this bromine compound to an experimental test.

If hydrochloric acid is used, instead of hydrobromic acid, for decomposing the hemiacetal, the product is a mixture of trichloroxyparaquinone with the tribrom compound in the proportion of about one part of the latter to three of the former. This replacement of bromine by chlorine under the influence of hydrochloric acid by warming on the steam bath in an open vessel is certainly striking. It should be remembered in this connection that, in the presence of a quinone, hydrochloric acid may be converted into free chlorine, but we do not think it probable that such a reaction takes place to any extent in this case, for the product is the oxyparaquinone and not the oxyhydroquinone as it would be if chlorine had been formed in quantity. We are inclined, therefore, to ascribe this replacement to the direct action of the hydrochloric acid.

Porter and one of us[1] thought a similar replacement of bromine by chlorine took place when the α-benzyl alcohol body,

[1] This Journal, 31, 112 (1904).

$C_6Br_4OOC_7H_7OHOOC_6Br_4$, was heated with hydrochloric acid, but, in this case, the product was a pyrocatechin, not an orthoquinone. The α-water body, under the same conditions, gave a considerable amount of bromine. The study of this curious replacement of bromine by chlorine will be continued in this laboratory.

EXPERIMENTAL.

Preparation of Tetrabromorthobenzoquinone.—The tetrabrompyrocatechin was prepared by the action of bromine on pyrocatechin dissolved in glacial acetic acid as described in previous papers[1] of this series, but its conversion into the orthoquinone was carried on by the following method, which is less expensive and gives better yields than the oxidation in glacial acetic acid solution formerly used in this laboratory. Thirty grams of tetrabrompyrocatechin were dissolved in 30–35 cc. of ethyl alcohol and the solution cooled with ice water; 8 cc. of fuming nitric acid, diluted with 50–60 cc. of glacial acetic acid, were added, and the mixture stirred vigorously. It was then allowed to stand 10 minutes when about two-thirds of the tetrabromorthoquinone had separated from the solution. This was filtered out, washed thoroughly with water, and dried on a porous plate. The filtrate from the crystals was diluted with 500 cc. of water, which precipitated the dissolved tetrabromorthoquinone, and this was filtered quickly, washed thoroughly with water, and dried as before on a porous plate. The yield varied from 26–27 grams, so that, at best, it was nearly 90.5 per cent of the theoretical, whereas with the older method 24 grams, that is, 80.4 per cent of the theoretical, were obtained. The melting point of our quinone varied from 146° to 150°, apparently according to the purity of the tetrabrompyrocatechin. The older process gave melting points from 145° to 150°, the true melting point being 150°–151°; our product, therefore, was pure enough for our purposes.

Tribrommethoxyorthoquinonemethylhemiacetal, $C_6Br_3OCH_3O(OCH_3OH)$. — This substance was formed as a secondary product in the preparation of the α compound, $(C_6Br_4O_2)_2CH_3OH$, by the action of cold methyl alcohol on

[1] THIS JOURNAL, **26**, 34 (1901); **34**, 460 (1905).

tetrabromorthoquinone. Its formation accounts for the small amount of hydrobromic acid always observed in making the α compound. It remained dissolved in the methyl alcohol after the α compound had crystallized out, and was obtained by evaporating these mother liquors either by heat or spontaneously, after which the yellow residue was crystallized from a mixture of equal parts of benzene and ligroin until it showed the constant melting point 138°.

The substance can be obtained as the principal product as follows: one part of tetrabromorthoquinone was boiled with 10–12 parts of methyl alcohol on the steam bath in a flask with a return condenser for one and a half to two hours. At the end of this time the solution had taken on a much lighter color, and then about 8 parts of the methyl alcohol were distilled off and the remainder allowed to evaporate. The residue was purified as before by crystallization from equal parts of benzene and ligroin, until it showed the constant melting point 138°, when it was dried *in vacuo* for analysis.

I. 0.3632 gram substance gave 0.3140 gram CO_2 and 0.0584 gram H_2O.

II. 0.3608 gram substance gave 0.3151 gram CO_2 and 0.0572 gram H_2O.

III. 0.1021 gram substance gave 0.1411 gram AgBr.

IV. 0.1383 gram substance gave 0.1910 gram AgBr.

	Calculated for $C_6Br_3OCH_3O(OCH_3OH)$.	Found. I.	II.	III.	IV.
C	23.59	23.58	23.82	. .	. .
H	1.72	1.80	1.77	. .	. .
Br	58.96	. .	. .	58.81	58.77

Properties of Tribrommethoxyorthoquinonemonomethylhemiacetal.—It crystallizes in yellow plates which melt at 138° to a colorless liquid. It is easily soluble in ethyl or methyl alcohol, ether, chloroform, benzene, toluene, or glacial acetic acid; slightly soluble in ligroin or in hot water, which gives a purple solution. Strong hydrochloric acid converts it into an orange product which will be described later; strong sulphuric acid dissolves it with a red color; strong nitric acid acts in the same way but more slowly; aqueous sodic hydrate acts on it at once, giving a dark orange color.

Tribrommethoxyorthoquinonemonomethylacetacetal, $C_6Br_3OCH_3O(OCH_3OC_2H_3O)$.—Three grams of the hemiacetal were heated with 15 cc. of acetic anhydride on the steam bath in a flask with a return condenser for half an hour. On cooling, nearly white crystals were deposited which were purified by crystallization from a mixture of equal parts of benzene and ligroin until they showed the constant melting point 158°, when they were dried *in vacuo* for analysis.

0.1678 gram of substance gave 0.2112 gram AgBr.

	Calculated for $C_6Br_3OCH_3O(OCH_3OC_2H_3O)$.	Found.
Br	53.45	53.56

Properties of Tribrommethoxyorthoquinonemonomethylacetacetal.—It crystallizes from a mixture of benzene and ligroin in slightly yellow crystals, apparently of the orthorhombic system, which melt at 158° to a colorless liquid. It is freely soluble in ether, acetone, benzene, or toluene; slightly soluble in ethyl alcohol, more so in methyl alcohol; practically insoluble in ligroin or water. Strong hydrochloric acid or strong nitric acid has no effect on it; strong sulphuric acid gives with it a red solution; sodic hydrate in aqueous solution decomposes it, forming an orange solution.

Tribrommethoxyorthoquinonemonomethylacetacetalhydrazone, $C_6Br_3OCH_3N_2HC_6H_5(OCH_3OC_2H_3O)$.—One gram of the methylacetacetal just described was mixed with 10 cc. of phenylhydrazine and the mixture, after being warmed on the steam bath for a few minutes, was allowed to stand overnight. The white, crystalline product thus obtained was washed very thoroughly with benzene and ligroin, ligroin, alcohol, and ether, and then dried *in vacuo* for analysis. This method of purification was adopted because the product seems to be decomposed when it is dissolved, the crystals formed having a reddish color.

0.0872 gram of substance gave 0.0901 gram AgBr.

	Calculated for $C_6Br_3OCH_3N_2HC_6H_5(OCH_3OC_2H_3O)$.	Found.
Br	44.52	43.97

Properties of the Tribrommethoxyorthoquinonemonomethylacetacetalhydrazone.—It crystallizes in nearly white needles

which melt at 205° to a red liquid. It is very slightly soluble in the common solvents, when cold, and, if heated with them, it is decomposed; thus, the solution in alcohol or benzene deposits reddish crystals. The three strong acids or sodic hydrate decompose it.

Tribromoxyparabenzoquinone, $C_6Br_3OHO_2$.—One gram of the tribrommethoxyorthoquinonehemiacetal was dissolved in a concentrated aqueous solution of hydrobromic acid and warmed on the steam bath for one hour. On cooling, red plates of the oxyparaquinone were deposited, which were purified by crystallization from a mixture of equal parts of benzene and ligroin until they showed the constant melting point 205°, when they were dried *in vacuo* for analysis.

0.1141 gram of substance gave 0.1784 gram AgBr.

	Calculated for $C_6Br_3OHO_2$.	Found.
Br	66.48	66.54

Properties of the Tribromoxyparaquinone.—It crystallizes in red plates which turn purple on exposure to the air and melt at 205°. It is freely soluble in ethyl or methyl alcohol; or ether, forming a purple solution; freely soluble in acetone, chloroform, benzene, or toluene with a reddish yellow color; slightly soluble in ligroin; soluble in water, forming a purple solution. Strong hydrochloric acid or hydrobromic acid dissolves it, apparently without alteration; strong nitric acid or sulphuric acid has no effect on it in the cold but decomposes it when hot; sodic hydrate dissolves it, forming a green solution, probably of the salt of the oxyquinone, which, on warming, turns purple from the formation of the chloranilate.

Action of Hydrochloric Acid on Tribrommethoxyorthoquinonehemiacetal.—If a few grams of the hemiacetal were dissolved in strong hydrochloric acid and the solution heated on the steam bath for half an hour, beautiful orange plates were deposited on cooling, which, after crystallization from a mixture of equal parts of benzene and ligroin, showed the constant melting point 195°. On submitting this substance to an analysis according to Carius, the argentic halide obtained was pure white and dissolved in ammonic hydrate with the utmost ease, showing

that it was in great part argentic chloride. It seemed, therefore, that part, at least, of the tribrom compound had been converted into the corresponding trichlor compound by the action of hydrochloric acid. That this change was not complete was shown by the melting point, 195°, instead of 198° for the pure $C_6Cl_3OHO_2$, and by the analyses, which came about 1.5 per cent lower than the value calculated for pure AgCl. This view was confirmed by the detection of a little bromine in the argentic halide. According to our calculations, it is a mixture of about 3 parts of the chlor compound with one of the brom compound, as shown by the following analysis, which was confirmed by two others.

0.1362 gram of substance gave 0.2500 gram of mixed halides.

	Calculated for $3C_6Cl_3OHO_2.C_6Br_3OHO_2$.	Found.
3Cl + Br	53.58	53.54

As was to be expected, the mixture resembled its two components in the strongest way in its properties; as did also the acet body formed from it, which melted at 113° instead of 127°, the melting point of the pure trichlor compound and, on analysis, also gave results indicating the presence of the two halogens.

We are at present continuing the study of the derivatives of tetrabromorthoquinone in several other directions.

CAMBRIDGE, MASS.,
August 4, 1907.

METHYLDINORMALPROPYLMETHANE.

BY LATHAM CLARKE.

A research on the hydrocarbons of the formula C_9H_{18} is now in progress in this laboratory. In the course of this investigation, all the possible isomers will be prepared and a study made of their chemical and physical properties. At the present time, five of the eighteen possible octanes have been synthesized, *viz.*, normal octane,[1] diisobutyl,[2] 3-methylheptane,[3] dimethyl-3-

[1] Riche: Ann. Chem. (Liebig), **117**, 265. Schorlemmer: *Ibid.*, **161**, 280; **147**, 227; **152**, 152. Zincke: *Ibid.*, **152**, 15. Paterno and Peratoner: Ber. d. chem. Ges., **22**, 467.

[2] Wurtz: Ann. Chem. (Liebig), **96**, 365. Schorlemmer: *Ibid.*, **114**, 188. Koch: *Ibid.*, **69**, 261.

[3] Welt: Ann. Chim. Phys., [7]. **6**, 121.

4-hexane,[1] and hexamethylethane.[2] Of the remaining thirteen, the first to be synthesized was 2-methylheptane, or methyldinormalpropylmethane, described in this paper.

The method which seemed best adapted for obtaining this octane in a state of highest purity was that given in the following series of reactions:

Methylnormalpropyl ketone was prepared from ethyl acetate by saponification; on reduction, this yielded methylnormalpropylcarbinol, which, in turn, was transformed into the corresponding carbinol iodide. The sodium salt of acetacetic ester was then treated with this iodide, giving ethyl β-amylacetacetate,

$$\begin{array}{l} CH_3COCHCO_2C_2H_5 \\ \quad\quad | \\ CH_3{-}CH{-}CH_2CH_2CH_3 \end{array}.$$

By saponification of this, β-amylacetone was obtained,

$$\begin{array}{l} CH_3COCH_2 \\ \quad\quad | \\ CH_3{-}CH{-}CH_2CH_2CH_3 \end{array}.$$

This was transformed into the corresponding carbinol and then into carbinol iodide which, by reduction, gave an octane having the structure

$$CH_3CH_2CH_2.CH(CH_3)CH_2CH_2.CH_3.$$

The whole series of reactions is concisely expressed in the following summary:

$CH_3CO\diagdown$
$\quad\quad\quad CH - CO_2C_2H_5$, Ethylacetacetic ester ➡
$C_2H_5\diagup$

$CH_3COCH_2C_2H_5$, Methylnormalpropyl ketone ➡

$CH_3CHOHC_3H_7$, Methylnormalpropylcarbinol ➡

$CH_3CHI.C_3H_7$, 2-Iodopentane ➡

$CH_3CH - C_3H_7$
$\quad\quad |$
$CH_3COCH - CO_2C_2H_5$, β-Amylacetacetic ester ➡

$(C_3H_7(CH_3)CH.CH_2.COCH_3$, 4-Methyl-2-heptanone ➡

$(C_3H_7)(CH_3)CH.CH_2CHOHCH_3$, 4-Methyl-2-heptanol ➡

$(C_3H_7)(CH_3)CH.CH_2CHI.CH_3$, 4-Methyl-2-iodoheptane ➡

[1] Norris and Green: THIS JOURNAL, **26**, 313 (1901).
[2] Henry: Compt. rend., **142**, 1075 (1906).

$(C_3H_7)(CH_3)CH.CH_2CH_2CH_3$, 4-Methylheptane or Methyldinormalpropylmethane.

EXPERIMENTAL.

Methylnormalpropyl Ketone.

Ethyl ethylacetacetate was made from ethyl acetacetate by Conrad's method.[1] It was found that in this reaction from 2 to 10 per cent of the diethyl derivative was always produced, but it was more convenient to postpone the separation of the two products until the corresponding ketones were obtained, when, by fractional distillation, the two derivatives were completely separated.

The impure ethyl ethylacetacetate was boiled for ten hours with 10 per cent caustic potash solution, using three molecules of potassic hydrate to one of the acetate. The mixture was then distilled with steam, the upper layer of the distillate separated, washed once with water, dried over calcic chloride, and fractionated with a long Hempel column. After five distillations, two portions were obtained, one boiling at 101.8° and the other at 138°; the first was methylnormalpropyl ketone, the second, 3-ethyl-2-pentanone. From 200 grams of the mixed ethyl acetacetate and diethyl acetacetate, 75 grams of the first ketone and 6 to 7 grams of the second were usually obtained.

Methylnormalpropylcarbinol.

This carbinol has been prepared by Friedel[2] and also by Belohoubek[3] by reduction of methylnormalpropyl ketone with sodium amalgam, but the reduction can be carried out much more satisfactorily by the method described in the following experiment:

190 grams of methylnormalpropyl ketone were dissolved in 360 grams of ether and the solution poured over 320 grams of water in a large flask provided with a long return condenser. 105 grams of sodium were added piece by piece, in the course of two or three hours, and when the reaction ceased, the ethereal layer was separated and fractionated. After three distillations, there were obtained 102 grams of a portion boiling at 119° under 760 mm. pressure and consisting of methylnormalpropyl-

[1] Conrad and Limpach: Ann. Chem. (Liebig), **192**, 153.
[2] Jahres. d. Chem., **1869**, 513.
[3] Ber. d. chem. Ges., **9**, 924.

carbinol, and 35 grams of a portion boiling at 220°–224° and consisting of symmetrical dimethyldipropylglycol. The yield of the carbinol was about 52.5 per cent of the theoretical.

2-Iodopentane.

Methylnormalpropylcarbinol was transformed into 2-iodopentane by allowing a mixture of 56 grams of carbinol, 70 grams of iodine, and 7 grams of red phosphorus to stand at room temperature for one hour, and then heating it on the water bath for three hours. The mixture was distilled, the iodide separated, washed with water and very dilute caustic potash solution, and dried over calcic chloride. The iodide was not redistilled. The yield in this experiment was about 104 grams.

Preparation of Ethyl β-Amylacetacetate.

It was found by experiment that Conrad's[1] method for the preparation of acetacetic ester derivatives worked very poorly with 2-iodopentane and ethyl acetacetate, the reaction yielding almost none of the expected product, but giving instead ethyl-β-amylether, propylethylene, and several other by-products. Accordingly, the following procedure was employed in the synthesis of ethyl β-amylacetacetate.

85 grams of ethyl acetacetate were dissolved in 200 grams of pure benzene, and 15 grams of sodium were added. Toward the end the sodium dissolved very slowly, although the reaction was carried out on the steam bath, and the few small pieces of sodium remaining undissolved after an hour were removed with a platinum spatula. To the solution were added 97.5 grams of 2-iodopentane, which is three-fourths the theoretical quantity demanded by the given weight of ethyl acetacetate, but these quantities were used because the 2-iodopentane was more valuable than the ethyl acetacetate and it was desirable, therefore, to get the best possible result from the former at the expense of some of the latter. The amount of sodium removed was so small (usually less than half a gram) that the sodium ethyl acetacetate was always present in excess.

The benzene solution of sodium ethyl acetacetate and 2-iodopentane was heated on the water bath with a reflux condenser

[1] *Loc. cit.*

for 15 hours, and then set aside for 5–6 hours. During this time the sodium iodide separated out and formed a layer on the bottom of the flask. The clear solution was decanted and then was heated on a calcic chloride bath (boiling point 120°) and about three-fourths of the benzol distilled off. The first runnings consisted of about one gram of a liquid boiling at 39°, which later was found to be propylethylene. This undoubtedly was formed from 2-iodopentane by the splitting off of hydriodic acid in the alkaline solution. Analysis gave the following result:

0.2995 gram substance gave 0.8570 gram CO_2 and 0.3861 gram H_2O.

	Calculated for C_5H_{10}.	Found.
C	85.71	85.84
H	14.28	14.32

Towards the end of the distillation considerable sodium iodide separated out and the solution was shaken vigorously to prevent bumping. The residue was treated with twice its volume of water. After standing a few minutes a copious crop of needles was deposited. Some separated out in the water, but in the benzol-ester mixture the needles were so thickly deposited that it became jellylike and could be almost inverted without spilling. The water was drawn off and filtered and the needles recrystallized from alcohol twice. The melting point was then constant at 169°.

The benzene solution was filtered and the needles were recrystallized twice from alcohol. The melting point, 169°, showed that they were identical with those obtained from the water. The yield of these crystals was four grams, thus showing that this body was only a small by-product.

Study of the White Needles.

Analysis gave the following results:

I. 0.1133 gram substance gave 0.2637 gram CO_2 and 0.0742 gram H_2O.

II. 0.1343 gram substance gave 0.3151 gram CO_2 and 0.0868 gram H_2O.

III. 0.1305 gram substance gave 0.3031 gram CO_2 and 0.0876 gram H_2O.

	Calculated for $C_{11}H_{18}O_4$.	Found. I.	II.	III.
C	63.30	63.46	63.77	62.91
H	7.37	7.27	7.15	7.45

These analyses show that the formula for the substance is $C_{11}H_{18}O_4$ or some multiple of this.

Properties.—This substance crystallizes from 95 per cent ethyl alcohol in long, fibrous, white needles; it is very soluble in hot alcohol but only moderately so in the cold. It is soluble also in acetone, acetic ester, benzol, and methyl alcohol; insoluble in water. It dissolves readily in aqueous caustic potash, giving a yellow solution which soon turns red. The yellow solution, when treated with dilute hydrochloric acid, precipitates the white substance unchanged, but when hydrochloric acid is added to the red solution after the latter has been boiled a few minutes, a red substance is thrown down which is entirely different from the original white body.

It is hoped that this interesting compound can be further studied within the next few months.

Ethyl β-Amylacetacetate.

The filtrate from the white crystals, after being dried over dehydrated potassic carbonate, was fractionated and yielded 56 grams of a liquid, boiling at 226° under 760 mm. pressure, which, as is shown later, was ethyl β-amylacetacetate. The yield was about 57 per cent of the theoretical amount as calculated from the weight of 2-iodopentane used.

The method of formation from 2-iodopentane and sodium ethylacetacetate proves that the formula for β-amylacetacetate is

$$\begin{array}{l} CH_3COCH—CO_2C_2H_5 \\ \quad\quad\quad | \\ CH_3CH—CH_2CH_2CH_3 \end{array} ;$$

This was further shown by analysis.

0.2074 gram substance gave 0.5063 gram CO_2 and 0.1781 gram H_2O.

	Calculated for $C_{11}H_{20}O_3$.	Found.
C	66.00	66.58
H	10.00	9.55

Properties.—This compound is an oily liquid boiling at 226° under 760 mm. pressure, has a pleasant characteristic odor like that of dandelions, and mixes with ether, ethyl alcohol, methyl alcohol, toluene, benzene, chloroform, and glacial acetic acid.

β-Amylacetone or 4-Methyl-2-heptanone.

Ethyl β-amylacetacetate was boiled for ten hours with three molecules of caustic potash, in ten per cent solution, in a large flask fitted with a reflux condenser; the resulting liquid was distilled with steam and the upper layer of the distillate separated, dried over calcic chloride, and distilled with a Hempel column. After three fractionations of the portion boiling at 150°–165°, practically all the liquid collected in one fraction boiling at 156° under 760 mm. of pressure. A small amount of unchanged ethyl β-amylacetate was usually found to be present after the treatment with alkali, but this was removed by the subsequent distillation. The fraction boiling at 156° was β-amylacetone or 4-methyl-2-heptanone,

$$CH_3COCH_2—\underset{\displaystyle CH_3}{\overset{\displaystyle |}{CH}}—CH_2CH_2—CH_3.$$

The usual yield was fifty per cent of the theoretical, 50 grams of ethyl β-amylacetacetate giving about 17 grams of the ketone.

Experiments with sulphuric acid as the hydrolyzing agent gave much poorer yields.

Analysis gave the following results:

0.1531 gram substance gave 0.4198 gram CO_2 and 0.1742 gram H_2O.

	Calculated for $C_8H_{16}O$.	Found.
C	75.00	74.78
H	12.50	12.64

Properties.—β-amylacetone boils at 156°, has a strong, pleasant, and very characteristic odor like that of bananas, and is soluble in ether, ethyl alcohol, methyl alcohol, benzene, toluene, chloroform, and glacial acetic acid.

4-Methyl-2-heptanol.

This compound was formed from β-amyl ketone by reduction in the following manner:

Four parts of ketone, by weight, were dissolved in eight parts of ether and poured over seven parts of water. Sodium, two parts, was added slowly in small pieces, and when the metal had completely dissolved the ethereal layer was separated and distilled. The ethereal residue, on fractionating, collected in two parts, one boiling at 160°–175° and the other, of which there was only a small quantity, boiling much higher, roughly between 285°–290°. The first fraction was redistilled three times and yielded a liquid boiling quite sharply at 168° under 762 mm. pressure. This was the carbinol,

$$\begin{array}{l} CH_3CHOH—CH_2 \\ \qquad\qquad\quad | \\ CH_3—CH—CH_2CH_2CH_3. \end{array}$$

The second fraction was not studied further, as the quantity at hand was small, but it was without doubt a pinacone having the formula

$$\begin{array}{l} CH_3C—(OH)—CH_2CH(CH_3)CH_2CH_2CH_3 \\ \quad | \\ CH_3—C—(OH)—CH_2—CH(CH_3)CH_2CH_2CH_3 \end{array}.$$

In a typical experiment, 16 grams of ketone yielded 14 grams of carbinol and one gram of pinacone. It will be noticed that the proportion of pinacone formed in this reaction is much smaller than is usual in such reductions. It was found that when the reduction took place rapidly the amount of pinacone produced was smaller than when the reduction was slow. In some cases, less than half a gram of pinacone was formed; in other cases, five grams were produced.

Analysis of 4-methyl-2-heptanol gave the following results:

0.1498 gram substance gave 0.4055 gram CO_2 and 0.1871 gram H_2O.

	Calculated for $C_8H_{18}O$.	Found.
C	73.85	73.82
H	13.85	13.88

Properties.—It boils at 168° under 762 mm. pressure, has an odor like dilute commercial amyl alcohol, and is soluble in ether, ethyl alcohol, methyl alcohol, benzene, toluene, chloroform, and glacial acetic acid.

Preparation and Reduction of 2-Iodo-4-methylheptane.

The carbinol just described was heated to 100° on the water bath and hydriodic acid gas[1] passed in until the saturation point was reached. After standing an hour, more hydriodic acid gas was passed into the liquid, which now consisted mainly of 2-iodo-4-methylheptane. This was neither distilled nor even washed with water, but was dissolved in an equal volume of methyl alcohol and the flask containing it connected to a return condenser. A few cubic centimeters of concentrated hydrochloric acid (38 per cent) and several grams of granulated zinc were added to the solution. The evolution of hydrogen began at once. The flask warmed up and was kept at a temperature of about 45° by immersing it in a bath of warm water. From time to time, sufficient hydrochloric acid was added to keep up a vigorous action and care was taken to have the zinc present in large excess. After the action had continued for several minutes, a floating oily layer began to separate out. This increased slowly and in about 15 hours seemed to have reached a maximum. It was separated, dried over calcic chloride, and distilled. The first fraction of the distillate consisted of a small amount of methyl alcohol; the second part came over between 110° and 125°; the portion boiling above 125° seemed to consist of unchanged carbinol and iodide. The heating was therefore stopped, the residue saturated with hydriodic acid gas, put back into the reduction flask, and the process repeated.

The fraction boiling at 110°–125° consisted principally of octane. It was shaken with concentrated sulphuric acid, then allowed to stand over concentrated sulphuric acid for two weeks, washed with aqueous caustic soda, and treated with metallic sodium. The liquid was kept over sodium for a month and was finally boiled for several hours with a return condenser.

[1] Prepared by the method described in Gatterman's "Pract. Meth. Org. Chem.," 2nd edition, p. 345.

This long treatment was found to be necessary to remove the last traces of halogen, which are held with great tenacity. The liquid, on distillation, boiled sharply at 118° under 760 mm. pressure and was found to be the octane methyldinormalpropylmethane, or 4-methylheptane. The yield was usually about 40 per cent of the theoretical.

Methyldinormalpropylmethane.

The hydrocarbon obtained by the reduction described above is a colorless, mobile liquid, almost odorless, and entirely free from halogen. Its constitution is proven beyond question by the method of its formation.

Analysis: 0.1449 gram substance gave 0.4466 gram CO_2 and 0.2097 gram H_2O.

	Calculated for C_8H_{18}.	Found.
C	84.21	84.05
H	15 79	16.08

Properties.—This octane boils sharply at 118° under 760 mm. pressure. At 15° its specific gravity is 0.7217. Its index of refraction, as determined by Mr. A. C. Boylston, who used a Pulfrich refractometer, is n D (25°) = 1.3978.

I am deeply indebted to the C. M. Warren fund for materials used in this research.

CAMBRIDGE, MASS.,
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ON THE DETECTION OF OZONE, NITROGEN PEROXIDE, AND HYDROGEN PEROXIDE IN GAS MIXTURES.

BY EDWARD H. KEISER AND LEROY MCMASTER.

When air is acted upon in a number of ways, such as by electric sparks, the flaming arc, burning hydrogen, burning magnesium, heated platinum wire, etc., in short, by any means which produce very high temperatures, ozone, nitrogen peroxide, and hydrogen peroxide may be formed. The silent electric discharge and the slow oxidation of phosphorus produce oxidizing gases in air. Several commercial processes of treating air so as to convert it into a more active chemical agent are at present in use. It is desirable, therefore, to have char-

acteristic reactions for each of the three substances above mentioned in examining the gases produced in these different ways.

A great many reagents have been suggested for this purpose but many of these have been found to be unreliable, while others are not very sensitive, and still others are rare substances that are not easily obtained. The following table contains a list of such substances, together with a statement of their behavior toward ozone, nitrogen peroxide, and hydrogen peroxide.

	Ozone.	Nitrogen peroxide.	Hydrogen peroxide.
Potassium iodide and starch[1]	blue	blue	blue
Wine-red litmus paper moistened with potassium iodide[2]	blue	no change	blue
Tetramethyl-paraphenylenediamine[3]	bluish violet	bluish violet	bluish violet
Metaphenylenediamine, alkaline solution[4]	Burgundy red or yellow	no change	no change
Manganese chloride paper moistened with guiacum tincture[5]	blue	blue	no change
Benzidine in alcohol[6]	brown	blue	no change
Tetramethyl-*p*-*p*-diaminodiphenylmethane in saturated alcoholic solution[7]	violet	yellow	no change
Potassium ferricyanide and ferric chloride[8]	no change	no change	blue

[1] Schoenbein: Ber. u. d. Verh. d. Nat. Ges., Basel, **4**, 58.
[2] Houzeau: Ann. Chim. Phys., [4], **5**, 20.
[3] Wurster: Ber. d. chem. Ges., **19**, 3195.
[4] Erlwein and Weil: *Ibid.*, **31**, 3158.
[5] Engler and Wild: *Ibid.*, **29**, 1940.
[6] Arnold and Mentzel: *Ibid.*, **35**, 1324.
[7] *Ibid.*
[8] Schoenbein, Weltzien, also Schoene: *Ibid.*, **7**, 1695. Engler and Wild: *Ibid.*, **29**, 1940.

	Ozone.	Nitrogen peroxide.	Hydrogen peroxide.
Manganese dioxide or copper oxide[1]	decomposed	no change	decomposed
Silver foil[2]	black	no change	no change
Chromic acid and ether[3]	no change	no change	blue
Chromic acid[4]	no change		decomposed
Titanium hydroxide in sulphuric acid[5]	no change	no change	yellow
Thallous salts[6]	brown	no change	no change
Ammonium molybdate in sulphuric acid[7]	no change	no change	yellow
Guiacum tincture with malt infusion[8]	no change	no change	blue
Gold chloride free from acid[9]	black	no change	
Nitrite test with sulphanilic acid and α-naphthylamine[10]	no change	pink	no change

Arnold and Mentzel[11] have studied a number of the reagents that are mentioned in the preceding list. They find that potassium iodide and starch, and zinc iodide and starch, as well as guiacum tincture, give a blue color with ozone, nitrogen peroxide, chlorine, and bromine. In short, these reagents are not characteristic of anything more than an oxidizing gas. Red litmus paper moistened with potassium iodide solution they find to be entirely unreliable, because all paper turns blue with free iodine, and any gas that liberates iodine will turn the paper blue. They also found that a solution of potassium iodide to

[1] Andrews and Tait: Ann. Chem. (Liebig), **112**, 135.
[2] Ber. d. chem. Ges., **35**, 1326.
[3] Barreswill: Ann. Chim. Phys., [3], **20**, 364.
[4] Engler and Wild: Ber. d. chem. Ges., **29**, 1940
[5] Schoenn: Z. anal. Chem., **9**, 41.
[6] Schoene: Ann. Chem. (Liebig), **196**, 58.
[7] Schoenn: Z. anal. Chem., **9**, 41.
[8] Struve: *Ibid.*, **8**, 274.
[9] Boettger: *Ibid.*, **19**, 105.
[10] Bull. Soc. Chim., [3], **2**, 347 (1889).
[11] Ber. d. chem. Ges., **35**, 1324.

which wine-red litmus solution had been added was unsatisfactory, because the ozone acts upon the litmus and changes it to a green color. The third reagent in the above list, tetramethyl-paraphenylenediamine, is also turned blue by all oxidizing gases. Metaphenylenediamine, the fourth one, was unsatisfactory because they found that nitrogen peroxide gave the same color as ozone, and all oxidizing gases give yellowish colors with this substance. Silver foil[1] is not satisfactory because it is not at all sensitive. Arnold and Mentzel recommend an alcoholic solution of benzidine or, still better, an alcoholic solution of tetramethyl-*p*-*p*-diaminodiphenylmethane. This gives a violet color with ozone and yellow with nitrogen peroxide; with hydrogen peroxide it remains unchanged. They found, however, that the ozone obtained by the action of sulphuric acid upon barium dioxide had a different action upon this reagent; instead of violet a green color was obtained. Benzidine, under the same conditions, gave a blue instead of a brown color. Similar effects were obtained with the ozone from persulphates, percarbonates, and from sodium and hydrogen peroxides.

F. Fischer and Marx[1] have used tetramethyl-*p*-*p*-diaminodiphenylmethane or "tetramethyl base," as it is called, in their investigations upon the formation of ozone and nitrogen peroxide in air at high temperatures. They prepared ozone by the silent electric discharge in the Siemen's ozonometer, by the action of ultraviolet light, by the electrolysis of sulphuric acid, and in other ways, and found that ozone produces with this reagent a violet color and the oxides of nitrogen a yellow color. Mixtures of both gases give a dirty brown color intermediate between violet and yellow. Another fact that they emphasize is that the paper must always be kept moist; if it becomes dry, ozone changes it to a yellow color. To detect very small quantities of nitrogen oxides in the presence of ozone they recommend that the gas be conducted into liquid air. The ozone will dissolve while the oxides of nitrogen will sep-

[1] Manchot and Kampschulte (Ber. d. chem. Ges., **40**, 2891) have recently shown that while silver foil is not at all sensitive at ordinary temperatures, it becomes much more so at 220°-240° C. For metallic mercury they found the temperature at which action was strongest to be 170° C.

[1] *Ibid.*, **39**, 2555.

arate as blue flakes. When the liquid air is then filtered, the frozen oxides of nitrogen remain upon the filter. The filtrate is allowed to boil, the air distils away, and the ozone remains. In this way both can be separately identified.

This method is open to the objection that liquid air is not readily obtained in many places. Likewise, the "tetra base" of Wurster and the "tetramethyl base" of Arnold and Mentzel are not easily obtainable substances. Moreover, the color changes are not always satisfactory. Thallous salts and titanic acid are not always at hand. We have now, however, devised a method which is free from these objectionable features and enables us to identify each of these three substances in the presence of the others.

We found that potassium permanganate, even in very dilute solution, is not decolorized by ozone. Nitrogen peroxide and hydrogen peroxide, on the other hand, both reduce it instantly. To identify ozone in gases that contain at the same time nitrogen peroxide and hydrogen peroxide it is only necessary to draw the gases through a solution of potassium permanganate; the nitrogen peroxide and the hydrogen dioxide will not pass through, while the ozone will, and can then be detected with potassium iodide and starch.

To detect nitrogen peroxide in the presence of ozone and hydrogen peroxide we take advantage of the fact that both ozone and hydrogen peroxide are decomposed when passed through a tube containing powdered manganese dioxide. Nitrogen peroxide passes through unchanged. Its presence can be shown by passing the gas, after it has gone over the manganese dioxide, into very dilute permanganate. If the latter is decolorized, nitrogen peroxide was present. A still more delicate test for nitrogen peroxide is this: pass the gas, which may contain ozone and hydrogen dioxide, directly into pure caustic soda, made from metallic sodium and nitrite-free distilled water, and then test the caustic soda solution for nitrites by the well-known sulphanilic acid and α-naphthylamine method.

Hydrogen dioxide can be identified in the presence of both ozone and nitrogen peroxide by passing the gas mixture into

a solution of potassium ferricyanide and ferric chloride. The yellow brown solution becomes green and then blue as more hydrogen dioxide passes in. This formation of Prussian blue is characteristic of hydrogen dioxide and is not produced by either ozone or nitrogen peroxide. This we have found by experiment.

I. Examination of the Gases Produced by Burning Hydrogen in Air.

We have tried our method in the examination of the gases produced by burning hydrogen in air. A jet of burning hydrogen was introduced into the end of a glass tube fifteen millimeters in diameter. A current of air was drawn into the tube by means of an aspirator. The gas passed from the tube through a moderately strong solution of potassium permanganate and then into a solution of potassium iodide and starch. This soon became blue, thus showing that ozone was formed by the hydrogen burning in a rapid current of air. The potassium permanganate wash bottle was then replaced by a tube forty centimeters in length, filled with powdered manganese dioxide. Between this tube and the aspirator, a wash bottle with a very weak solution of potassium permanganate was inserted. Air was now rapidly drawn through the apparatus and the products of combustion of the hydrogen passed first over the manganese dioxide and then into the dilute permanganate. The latter, after a time, became decolorized, thus showing that nitrogen peroxide was formed. This was confirmed by passing the gases formed by burning hydrogen into a solution of nitrite-free caustic soda and then applying the nitrite test (Griess test) after having slightly acidified the solution. The pink color was formed, thus confirming the result obtained with dilute permanganate. The gases formed by burning hydrogen were also tested for hydrogen peroxide by drawing them through a solution of potassium ferricyanide and ferric chloride. This became first green, then blue, thus showing that hydrogen peroxide was present. This ferricyanide and ferric chloride test for hydrogen peroxide we found to be more sensitive than titanium dioxide in sulphuric acid.

The latter failed to show the presence of hydrogen peroxide in the gases produced by burning hydrogen in air.

II. Examination of the Gases Produced by the Silent Electric Discharge in Air and Oxygen.

Atmospheric air was purified and dried by being drawn, by means of an aspirator, through a series of wash bottles containing silver sulphate, potassium permanganate, and pure concentrated sulphuric acid, and was then passed through a Siemens' ozonometer. The ozonometer was connected with the terminals of a Ruhmkorff coil which, in turn, was connected with a storage battery. The potential of the coil discharge terminals was 2160 volts. The air passing through the ozonometer in which the silent discharge was taking place was thereupon conducted through a very weak solution of potassium permanganate. No decolorization took place, although the ozonized air was passed for more than two hours. Ozone was shown to be present in quantity, not only by its action upon potassium iodide and starch after it had passed through the permanganate, but also by its odor and by the repeated perforation of the rubber tube that connected the last wash bottle with the aspirator. We were surprised to find that, under these conditions, no nitrogen peroxide was formed. A quantitative determination of the ozone showed that there was 0.00086 gram per liter. We also conducted the air directly from the ozonometer into pure caustic soda and tested this for nitrites by the Griess test but failed to obtain any. With potassium ferricyanide and ferric chloride the ozonized air failed to give a reaction for hydrogen peroxide. The same results, namely, the absence of nitrogen peroxide and hydrogen peroxide in air that had passed through the Siemens' ozonometer, were obtained when we omitted washing the air with silver sulphate, caustic soda, potassium permanganate, and sulphuric acid before it entered the ozonometer. These experiments show conclusively that it is possible to ozonize air without, at the same time, forming nitrogen peroxide and hydrogen peroxide. We have repeated the above experiments with oxygen, made from fused sodium peroxide and water, instead of air. We obtained

no nitrogen peroxide nor hydrogen peroxide. A quantitative determination showed the presence of 0.0012 gram of ozone to the liter. This ozonized oxygen failed to decolorize potassium permanganate solution.

III. Examination of Gases Produced by the Action of Concentrated Sulphuric Acid upon Barium Dioxide.

Concentrated sulphuric acid was allowed to drop upon barium dioxide, contained in an Erlenmeyer flask, and the gases resulting were conducted through a concentrated solution of potassium permanganate in a Geissler potash bulb and then into a solution of potassium iodide and starch. A blue color soon appeared, thus showing the presence of ozone. The gas, after passing over manganese dioxide and then into permanganate, failed to give the reaction for nitrogen peroxide. Nor were we able to detect hydrogen peroxide by passing the gas through a solution of potassium ferricyanide and ferric chloride.

A small quantity of barium nitrate was now added to the barium dioxide and, on treating with concentrated sulphuric acid and testing as before, we obtained evidence of the presence of ozone and nitrogen peroxide, but not of hydrogen peroxide, in the gases given off.

IV. Examination of the Gases Produced by the Slow Oxidation of Phosphorus in Moist Air.

We have also used our method for the examination of the gases formed by the slow oxidation of phosphorus in air in the presence of water. We found ozone and nitrogen peroxide but no hydrogen peroxide.

V. Examination of the Gases Produced by the Action of the Flaming Electric Arc upon Air.

Air that had passed through the flaming electric arc of an Alsop process machine, such as is used in treating flour, was next examined by our method. We found that this air contained nitrogen peroxide, a trace of ozone, and a little hydrogen peroxide.

VI. Examination of Atmospheric Air.

We have applied our method to the examination of country air. Air from outside of the laboratory was drawn through a layer of absorbent cotton, six inches in length, then through a concentrated solution of potassium permanganate in a potash bulb, and finally into potassium iodide and starch. After the air had passed through for five hours, a faint blue color appeared, thus showing the presence of ozone. Air that was filtered through absorbent cotton and that had passed over a layer of manganese dioxide eighteen inches in length was conducted through a very faintly pink solution of permanganate. No decolorization was observed, although the air was drawn through for eighteen hours. We conclude from this that there was no nitrogen peroxide in the air. Air filtered through cotton was drawn through a solution of potassium ferricyanide and ferric chloride. After four hours the solution acquired a green color. We found, however, that the reagent used for detecting hydrogen dioxide, namely, a dilute solution of ferric chloride and potassium ferricyanide, when allowed to stand in air, gradually forms a green precipitate, even when protected from dust by being covered with a bell jar. We, therefore, drew atmospheric air for five hours through pure distilled water, contained in a potash bulb, and then tested this water with the reagent. We obtained no blue precipitate and, therefore, conclude that the green color mentioned above may not have been caused by hydrogen dioxide. These experiments prove that our method is sufficiently sensitive to show the presence of ozone in atmospheric air.

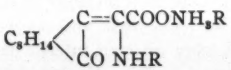
CHEMICAL LABORATORY,
WASHINGTON UNIVERSITY,
ST. LOUIS, April, 1907.

STUDY OF THE ACTION OF CERTAIN SECONDARY AMINES ON CAMPHOROXALIC ACID.

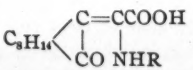
[ELEVENTH COMMUNICATION ON CAMPHOROXALIC ACID DERIVATIVES.[1]]

BY J. BISHOP TINGLE AND L. F. WILLIAMS.

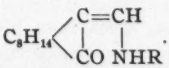
In the course of an investigation by Bishop Tingle and Hoffman,[2] it was found that dimethylamine and diethylamine condense with camphoroxalic acid. The products consist, empirically, of 1 molecule of acid + 2 molecules of base, no water being eliminated. Compounds of secondary bases and ketones or enols had not, hitherto, been prepared. Consequently the bodies in question possessed a special interest and made us anxious to elucidate the subject more fully. We also wished to throw some light on the constitution of these substances. On comparing them with the condensation compounds of camphoroxalic acid and primary amines, it is seen that their constitution presents a decided peculiarity. Bishop Tingle and his coworkers have shown[3] that this acid condenses with primary amines, forming derivatives belonging to one of the three following types:



I.



II.



III.

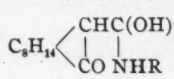
From what has been said above, it will be apparent that the compounds from secondary amines resemble, in general, type I., but differ from it by containing, in addition, the elements

[1] The previous papers on this subject have appeared as follows: Inaug. Diss., (Munich), 1889, p. 34. J. Chem. Soc., **57**, 652 (1890). THIS JOURNAL, **19**, 393 (1897); **20**, 318 (1898); **21**, 238 (1899); **23**, 214 (1900). J. Am. Chem. Soc., **23**, 363 (1901). THIS JOURNAL, **34**, 217 (1905); **36**, 223 (1906).

[2] THIS JOURNAL, **34**, 217 (1905).

[3] *Loc. cit.*

of water. It has been shown in previous papers that in all probability substances of type I. are formed by the addition of the primary amine to the double linkage and also in some cases to the carboxyl group, giving the intermediate compound,



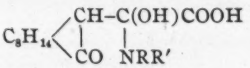
As a rule, these intermediate bodies are unstable and readily eliminate water, passing into substances of type I.

Some of them, however, are quite stable. A number of these have been described in previous papers by the senior author and his coworkers,[1] and we ourselves have obtained two others, from ethylenediamine and paraminophenol, respectively, in the course of some work on primary amines and camphoroxalic acid. A paper on this investigation will be published in an early number of THIS JOURNAL. On account of the presence of the extra molecule of water in these substances, they have received the name of *camphoformolamine derivatives.*

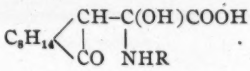
With regard to the compounds of the secondary amines and camphoroxalic acid, it is not unnatural to suppose that they might be representatives of this intermediate, additive form. There are two reasons which, at present, lead us to reject this view of their constitution. The first and most important is based on the fact that they give an intense violet coloration with ferric chloride and alcohol. Compounds of types I. and II., from the primary amines, and also the addition products of these amines which have just been referred to, give no color with this reagent, whereas camphoroxalic acid itself gives a deep red color. It is well known that these pronounced colorations are characteristic of the group C:COH, consequently, although the derivatives of the secondary amines must, no doubt, differ from the parent acid, yet they must contain the group in question. A second consideration leading towards the same conclusion is this: Secondary aliphatic amines are, in general, more strongly basic than the corresponding primary compounds. Other things being equal, the readiness with which

[1] *Loc. cit.*

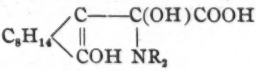
water is eliminated from a compound is decreased by the presence of negative groups in the molecule. Consequently, in so far as this reasoning is applicable to the case in question, the compound



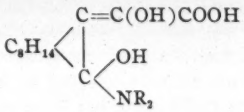
should eliminate the elements of water *more* readily than a substance with the constitution



Actually, of course, the exact opposite is found to be the case. These considerations lead us, therefore, to the formula



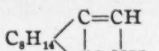
as the best expression of the constitution of the compounds of camphoroxalic acid and the secondary amines. As in the case of almost all the derivatives of this acid which have been studied, it is based upon the assumption that the primary point of attack is the C:COH group. The grounds on which this belief is based have been fully discussed by Tingle and Robinson,[1] and need not be repeated here. Should subsequent work ever show them to be invalid, the only change which would be involved in the formulas given above would be the representation of the nitrogen atom as being linked to the ketonic instead of to the enolic carbon atom, thus

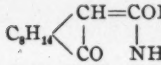


The question at once arises as to the designation of these compounds. Until their constitution is definitely established, it appears to us that the simplest plan is to term them *iso-*

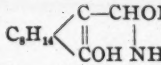
[1] This Journal, **36**, 223 (1906).

camphoformolamine derivatives; we have, then, three series of substances derived from the following complexes, *viz.*:


camphoformeneamine;


, *camphoformolamine*;

and

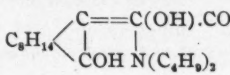

, *isocamphoformolamine.*

When these isocamphoformolaminecarboxylic acids, or their salts, are heated above their melting points, water and carbon dioxide are evolved, and products are obtained which are without action on ferric chloride and which resemble closely, in general properties, the compounds prepared, under corresponding conditions, from the condensation products of camphoroxalic acid and primary amines. They have, therefore, been formulated, in a manner similar to these latter, as alkyl or aryl derivatives of type III. given above. The secondary amines resemble the primary ones in that the ability of any individual one of them to form derivatives of both the isocamphoformolamine type or of type III. differs for each amine. This point is discussed more fully elsewhere in the present paper, *vide* p. 111.

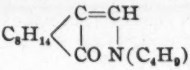
The first object of the investigation described in this paper was to apply the reaction discovered by Tingle and Hoffman to a number of other secondary amines. This has been done with a very considerable measure of success. The second object which we had in view was to obtain more experimental evidence for the formula which we have assigned to the compounds in question. This part of the work has been seriously interfered with by lack of the needed material which, though ordered early, did not reach us until too late to be of much use during the last academic year. The compounds named below have been studied. The nomenclature employed for the desig-

nation of the products of the reactions has been fully elucidated in the article by Tingle and Hoffman.[1]

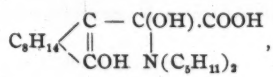
1. Diisobutylamine and camphoroxalic acid give *diisobutylisocamphoformolaminecarboxylic acid*,



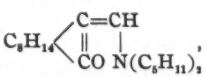
When this is heated above its melting point it forms *diisobutylcamphoformeneamine*,



2. Diamylamine gives *diamylisocamphoformolaminecarboxylic acid*,

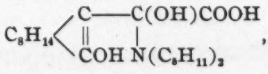


which forms *diamylcamphoformeneamine*,

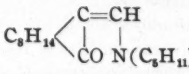


when heated above its melting point.

3. Diisoamylamine gives *diisoamylisocamphoformolaminecarboxylic acid*,



which is converted into *diisoamylcamphoformeneamine*,

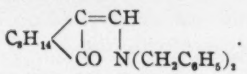


when heated above its melting point.

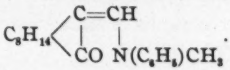
4. Dibenzylamine and camphoroxalic acid react with greater

[1] *Loc cit.*

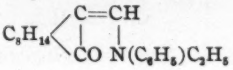
difficulty than the amines mentioned above. The product is *dibenzylcamphoformeneamine*,



5. Methylaniline and camphoroxalic acid also react with some difficulty, forming *phenylmethylcamphoformeneamine*,

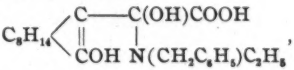


6. Ethylaniline gives *phenylethylcamphoformeneamine*,

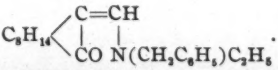


a viscous liquid.

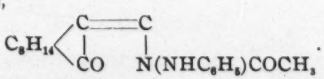
7. Benzylethylamine gives *benzylethylisocamphoformolaminecarboxylic acid*,



which, when heated above its melting point, is changed to *benzylethylcamphoformeneamine*,



8. Acetylphenylhydrazine gives *acetylphenylaminecamphoformeneamine*,

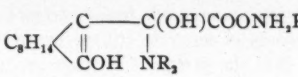


The conduct of the following acyl secondary bases towards camphoroxalic acid was studied:

Paranitrobenzoylparaminophenol, diparanitrobenzoylparaminophenol, metanitrobenzoylparaminophenol, dimetanitrobenzoylparaminophenol, paranitrobenzoylorthoaminophenol, diparanitrobenzoylorthoaminophenol, metanitrobenzoylorthoaminophenol, dimetanitrobenzoylorthoaminophenol, phenylsulphoneparaminophenol, phenylsulphoneorthoaminophenol, diphenylsulphoneorthoamino-

phenol, and *paracetoaminophenol*. No single one of these acyl derivatives could, however, be induced to undergo reaction. Besides these we also investigated the behavior of *benzoylphenylhydrazine*, *benzylphenylhydrazine*, *benzylmethylamine*, *benzylaniline*, *phenylhydrazine-p-sulphonic acid*, *phenyl-β-naphthylamine*, and symmetrical *phenylmethylhydrazine*. These compounds also failed to react.

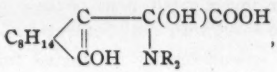
The preceding results permit of some rather interesting conclusions being drawn. In the case of the dimethyl- and diethylamine *two molecules* combine with *one* of camphoroxalic acid, forming a salt of the isoformolaminic acid,



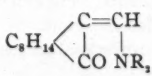
The remaining *aliphatic amines* which we have tried yield directly the *free acid* corresponding to the above salt. Tingle and Hoffman[1] were unable to prepare, from the salts of the dimethyl and diethyl compounds, the corresponding free acids. According to the system of nomenclature suggested by us, their two compounds should be termed *isocamphoformolamine*, not *camphoformolamine*, derivatives.

Evidently, therefore, the entrance of the more strongly basic, higher alkyl amine radical into the molecule of camphoroxalic acid has so weakened its acidic properties as to render it essentially a neutral body, incapable of salt formation. The gradation is a very interesting and delicate one.

In the case of the alkyl aniline derivatives which are, of course, feebler bases than the aliphatic amines, the acid type,



is rendered too unstable to be isolated, carbon dioxide and water are evolved spontaneously, and neutral products of the formula



[1] *Loc. cit.*

are formed. The same is true of the condensation products of acetylphenylhydrazine and of dibenzylamine, which react like the alkyl anilines, whereas ethylbenzylamine reacts exactly like the aliphatic amines.

In the case of benzylaniline and of β-naphthylaniline, it is evident that the basic properties are too feeble to permit of condensation taking place under the most favorable conditions which we were able to employ. We do not think that our results lend any definite support to a theory of spatial hindrance, but it would be difficult to obtain a clearer or more delicate representation of the changes in the nature of the amines.

The condensation compound from acetylphenylhydrazine deserves a few words of separate treatment, not only because we believe that it is the *first* condensation product which has ever been obtained from this amine, but also because we think that it is the first acylated amine which has been induced to react with a ketonic or enolic compound. We have made a number of experiments to elucidate its constitution more fully. Although it apparently undergoes hydrolysis rather readily, it is difficult to purify the resulting compound unless the experimental conditions under which it is formed are regulated very carefully. The work in this connection will be continued by the senior author.

The failure to obtain a similar condensation compound from camphoroxalic acid and benzoylphenylhydrazine is, no doubt, to be ascribed to the more strongly negative nature of the benzoyl, as compared with the acetyl, group.

Of the remaining acylated amines (acylated aminophenols) which have been investigated, none of them showed any signs of a tendency to react with camphoroxalic acids.

At present it is unnecessary to discuss further these negative results, except to point out that the substances in question, if they exhibit basic properties at all, do so to an extremely slight degree. Their behavior confirms, therefore, the observations and conclusions made by ourselves and also by Bishop Tingle and his coworkers on the amine derivatives of camphoroxalic acid.

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Secondary amines.	I. $C_8H_{14}\langle \overset{COH}{\underset{NR_2}{C}} \!\!=\!\!\!- C(OH)CO_2NH_2R_2$	II. $C_8H_{14}\langle \overset{COH}{\underset{NR_2}{C}} \!\!=\!\!\!- C(OH)CO_2H$	III. $C_8H_{14}\langle \overset{C:CH}{\underset{CO\ NR_2}{}}$	IV. $C_8H_{14}\langle \overset{C:CCO_2H}{\underset{CO\ NHR}{}}$
1. $NH(CH_3)_2$	137°.5*	.....	163°*	
2. $NH(C_2H_5)_2$	139°.5*	.....	153°*	
3. $NH(C_3H_7)_2$ *iso*	.....	180°	73°–74°	
4. $NH(C_4H_{11})_2$ *iso*	.....	160°	43°	
5. $NH(CH_2C_2H_5)_2$	.....	156°	40°	
6. $C_4H_8NHCH_3$	.....	.....	152°	
7. $C_4H_8NHC_2H_5$	.....	.....	126°	
8. $C_4H_8NHC_2H_5$	.....	.....	boils 285° (110 mm.)	
9. $C_4H_8CH_2NHC_6H_5$	.....	158°	57°	
10. $CH_3CONHNHC_6H_5$	.....	.....	174°	
11. $OC(NHCH_3)_2$	.....	.....	.....	104°–105°*
12. $C_6H_5C(NH_2):NH$	.....	.....	Yields compound $C_{13}H_{12}O_4N_2$ 184°*	

The foregoing table gives the type formulas and melting points of all the compounds of camphoroxalic acid and secondary amines which have been prepared hitherto. Those described before the appearance of this paper are marked.* The derivative of symmetrical dimethylcarbamide is included, although it is a derivative of a primary amine, because the parent substance is a secondary amine. Benzamidine may be regarded as being a secondary amine and, therefore, its derivative has also been given.

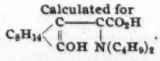
EXPERIMENTAL.

1. *Diisobutylamine.*

Diisobutylamine (2.9 grams = 1 molecule) and camphoroxalic acid (5 grams = 1 molecule) were dissolved in absolute ethyl alcohol and heated on the water bath for fifteen minutes. On cooling, crystals were deposited. These were purified by recrystallization from ethyl acetate, from which they separate in glistening, white needles, melting at 179°–180° with evolution of gas. With alcoholic ferric chloride the violet color, characteristic of the enolic grouping, is produced. Analysis of this compound showed it to be *diisobutylisocamphoformolaminecarboxylic acid.*

Analysis:

0.2078 gram substance gave 7.4 cc. N at 780 mm. and 21°.

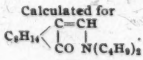


	Calculated for	Found.
N	3.97	4.08

When this substance is heated above its melting point, water and carbon dioxide are eliminated and a gum is left. This is purified by dissolving it in acetone; it deposited in white plates, melting at 73°–74°. With alcoholic ferric chloride no color reaction is produced. Analysis showed this compound to be *diisobutylcamphoformeneamine.*

Analysis:

0.1043 gram substance gave 4.4 cc. N at 760 mm. and 24°.



	Calculated for	Found.
N	4.81	4.61

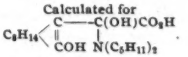
2. Diamylamine.

Diamylamine (7 grams = 2 mol.) and camphoroxalic acid (5 grams = 1 mol.) were heated in absolute alcoholic solution on the water bath. On cooling, crystals were deposited which were found to be readily soluble in methyl and ethyl alcohols, ethyl acetate, acetone, ether, and benzene. The compound was purified by recrystallizing from acetone. It separated in white, microscopic crystals melting at 160°. A violet color is produced by dissolving it in alcohol and adding ferric chloride. The compound dissolves in sodium bicarbonate solution with evolution of gas. Analysis showed the substance to be *diamylisocamphoformolaminecarboxylic acid.*

Analysis:

I. 0.1713 gram substance gave 0.4360 gram CO_2 and 0.1644 gram H_2O.

II. 0.2912 gram substance gave 9.4 cc. N at 762 mm. and 24°.

	Calculated for 	Found. I.	II.
C	69.23	69.41	. .
H	10.30	10.66	. .
N	3.68	. .	3.54

Diamylamine and camphoroxalic acid were also brought together under the following conditions: Camphoroxalic acid (2 grams = 1 mol.) was dissolved in alcohol and with this was mixed an amount of potassium hydroxide nearly sufficient to neutralize it. Diamylamine (1.4 grams = 1 mol.) was now added and the solution concentrated. After this heating, the liquid was rendered barely acid with dilute hydrochloric acid and the crystals which formed were recrystallized from acetone. The purified product was found to be identical with the compound described above.

When this substance is heated above its melting point in a tube connected with a vessel containing baryta water, carbon dioxide is given off, as is shown by the formation of barium carbonate. Water is also eliminated.

The resulting gummy material was treated with benzene and ligroin, and crystals were formed. Recrystallization from

acetone and then from ethyl acetate resulted in the deposition of white plates melting at 43°. It was difficult to free these crystals from gum although they were subjected to the action of various solvents a number of times. Analysis indicated that the compound was *diamylcamphoformeneamine.*

Analysis:

0.1715 gram substance gave 6.4 cc. N at 753 mm. and 24°.

	Calculated for $C_8H_{14}\langle \begin{matrix} C=CH \\ | \quad | \\ CO \quad N(C_5H_{11})_2 \end{matrix}$	Found.
N	4.40	4.04

3. Diisoamylamine.

Diisoamylamine (3.2 grams = 2 mol.) and camphoroxalic acid (2.5 grams = 1 mol.) were dissolved in alcohol and heated till nearly all the solvent was evaporated. Ligroin was then added to the mixture and, on standing, crystals separated. These were purified by recrystallization from acetone, being deposited in white, microscopic crystals melting at 156°. In alcoholic solution a violet color is produced with ferric chloride. The compound dissolves in aqueous sodium bicarbonate solution with evolution of gas. Analysis showed it to be *diisoamylisocamphoformolaminecarboxylic acid.*

Analysis:

0.1917 gram substance gave 6.4 cc. N at 760 mm. and 25°.

	Calculated for $C_8H_{14}\langle \begin{matrix} C \quad\quad C(OH)CO_2H \\ \| \quad\quad | \\ COH \quad N(C_5H_{11})_2 \end{matrix}$	Found.
N	3.68	3.62

When the above compound is heated above its melting point, water and carbon dioxide are eliminated and a gummy mass is left in the tube. This material was purified by recrystallizing from ethyl acetate, being deposited in whitish, rather ill-defined crystals melting at 40°. With alcoholic ferric chloride there is no color reaction. Analysis showed this substance to be *diisoamylcamphoformeneamine.*

Analysis:

0.1400 gram substance gave 5.4 cc. N at 757 mm. and 25°.

	Calculated for $C_8H_{14}\langle \overset{C=CH}{\underset{CO}{|}} \overset{|}{\underset{N(C_6H_{11})_2}{|}}$.	Found.
N	4.40	4.17

4. Dibenzylamine.

Dibenzylamine (4 grams = 1 mol.), camphoroxalic acid (4.6 grams = 1 mol.), and absolute ethyl alcohol (30 cc.) were heated under pressure, at 130°, for 3 hours, the air in the tube being replaced with illuminating gas. Pressure was noticed in the tube when it was opened and crystals separated on agitating the solution. These were purified by recrystallizing from ethyl acetate and then from alcohol. The compound is deposited in small, glistening, white crystals, melting at 152°.

With alcoholic ferric chloride no color is produced.

Analysis showed this compound to be *dibenzylcamphoformeneamine.* Analysis:

I. 0.1531 gram substance gave 0.4690 gram CO_2 and 0.1182 gram H_2O.

II. 0.1989 gram substance gave 7.0 cc. N at 763 mm. and 25°.

	Calculated for $C_8H_{14}\langle \overset{C=CH}{\underset{CO}{|}} \overset{|}{\underset{N(CH_2C_6H_5)_2}{|}}$.	Found. I.	Found. II.
C	83.56	83.54	. .
H	8.07	8.57	. .
N	3.90	. .	3.83

5. Methylaniline.

Methylaniline (4.3 grams = 1 mol.), camphoroxalic acid (9 grams = 1 mol.), and benzene (50 cc.) were heated under pressure, at 120°, for 5 hours. Upon evaporating the excess of benzene a gummy mass remained, from which no crystals could be separated by the use of various solvents, the product always depositing from solution as a gum. This gum was, therefore, treated with an aqueous sodium carbonate solution and then extracted with ether. Upon acidifying the carbonate solution with dilute hydrochloric acid, free camphoroxalic acid was precipitated.

The ether solution, when evaporated, deposited crystals which were purified by recrystallization from ethyl acetate,

separating in slightly yellow, tetrahedral forms, melting at 126°. With alcoholic ferric chloride no color is produced. Analysis of this compound showed it to be *phenylmethylcamphoformeneamine.* Analysis:

I. 0.1053 gram substance gave 0.3099 gram CO_2 and 0.0864 gram H_2O.

II. 0.1102 gram substance gave 5.3 cc. N at 770 mm. and 24°.

	Calculated for $C_8H_{14}\langle^{C=CH}_{CO\ N(C_6H_5)CH_3}$	Found. I.	II.
C	80.23	80.26	. .
H	8.61	8.92	. .
N	5.21	. .	5.33

6. Ethylaniline.

Ethylaniline (2.15 grams = 1 mol.), camphoroxalic acid (4 grams = 1 mol.), and benzene (40 cc.) were heated under pressure, at 120°, for 5 hours. About half the benzene was then evaporated and ligroin added to the solution. On standing, a gum was deposited. This was then treated with sodium carbonate solution in the manner described in the preceding section, and extracted with ether. When the carbonate solution was acidified with dilute hydrochloric acid, camphoroxalic acid was precipitated.

Upon evaporating the ether solution, a liquid was left and, as it could not be induced to form crystals, it was finally distilled under diminished pressure. Two fractions were obtained. The first, boiling at 140°–145° (110 mm.), was found to be ethylaniline. The second fraction boiled at 285° (110 mm.) and is a deep yellow, viscous liquid. Analysis showed this to be *phenylethylcamphoformeneamine.* Analysis:

I. 0.2247 gram substance gave 0.6580 gram CO_2 and 0.1804 gram H_2O.

II. 0.2253 gram substance gave 10.4 cc. N at 770 mm. and 24.5°.

	Calculated for $C_8H_{14}\langle^{C=CH}_{CO\ N(C_6H_5)C_2H_5}$	Found. I.	II.
C	80.50	79.86	. .
H	8.89	8.92	. .
N	4.95	. .	5.10

7. *Benzylethylamine.*

Benzylethylamine (4.5 grams = 1.5 mols.) and camphoroxalic acid (5 gram = 1 mol.) were mixed and heated in absolute ethyl alcoholic solution on the water bath for 15 minutes. On cooling, crystals were deposited. These were purified by recrystallizing from ethyl acetate and were deposited in fine, white, flocculent crystals melting at 158° with evolution of gas. With alcoholic ferric chloride solution, a violet color is produced. The compound dissolves in sodium bicarbonate solution with evolution of gas. Analysis showed this substance to be *benzylethylisocamphoformolaminecarboxylic acid.* Analysis:

I. 0.1329 gram substance gave 0.3423 gram CO_2 and 0.1007 gram H_2O.

II. 0.1506 gram substance gave 5.5 cc. N at 758 mm. and 24°.

	Calculated for $C_8H_{14}\langle \overset{C}{\underset{COH}{\overset{\|}{\underset{\|}{}}}} \overset{C(OH)CO_2H}{\underset{N(CH_2C_6H_5)C_2H_5}{}} \rangle$.	Found. I.	Found. II.
C	70.13	70.24	. .
H	8.13	8.42	. .
N	3.89	. .	3.99

When this compound is heated above its melting point, in a tube connected with a vessel containing baryta water, carbon dioxide is eliminated, as is shown by the formation of barium carbonate in the liquid. Water also is given off. After cooling, a yellow gum was left. As no crystals could be separated by use of ordinary solvents, this gum was treated with sodium carbonate and the solution extracted with ether. A yellow oil was left after evaporating the ether. This solidified on standing. It was redissolved in alcohol and from this solution white crystals are deposited which melt at 57°. With ferric chloride and alcohol no color reaction is produced. Analysis showed the compound to be *benzylethylcamphoformeneamine.*

Analysis:

0.1867 gram substance gave 7.7 cc. N at 760 mm. and 23°.

	Calculated for $C_8H_{14}\langle \overset{C=CH}{\underset{CO}{\overset{\|}{\underset{\|}{}}}} \overset{}{\underset{N(CH_2C_6H_5)C_2H_5}{}} \rangle$.	Found.
N	4.72	4.54

8. Acetylphenylhydrazine.

Acetylphenylhydrazine (4.5 grams = 1 mol.), camphoroxalic acid (6.75 grams = 1 mol.), and benzene (30 cc.) were heated under pressure, at 140°–145°, for 14 hours. A considerable pressure was noticed when the tube was opened. When the benzene solution was evaporated, a tarry mass was formed from which no crystals could be separated by the use of various solvents; consequently, the tar was treated with sodium carbonate solution. The part insoluble in the carbonate solution was dissolved in benzene, and ligroin was added. On standing for several days crystals were deposited. These were recrystallized from ethyl acetate several times and then from ethyl alcohol, because the last traces of impurity were difficult to remove. The compound was finally deposited from alcohol in white needles melting at 174°. With alcoholic ferric chloride solution no color reaction is produced. Analysis showed it to be *acetylphenylaminecamphoformeneamine*. Analysis:

I. 0.1110 gram substance gave 0.2970 gram CO_2 and 0.0824 gram H_2O.

II. 0.1074 gram substance gave 9.1 cc. N at 758 mm. and 24°.

	Calculated for $C_8H_{14}\begin{matrix}C{=}CH\\ |\\ CO\,N(COCH_3)NHC_6H_5\end{matrix}$.	Found I.	Found II.
C	73.07	72.97	. .
H	7.68	8.24	. .
N	8.97	. .	9.24

Some of this compound was heated with potassium hydroxide solution of medium concentration for 3 hours, and then allowed to stand for 40 hours at the room temperature. The solution was now made acid with hydrochloric acid and extracted with ether. The crystals deposited from the ether solution were found to be unchanged material.

A second portion of the substance was then heated with somewhat dilute hydrochloric acid, 2 parts of concentrated acid to 1 part of water, for 3 hours and allowed to stand at the room temperature for 40 hours. The solution was then diluted with water and extracted with ether. From the ether

solution, crystals are deposited. They were recrystallized from acetone and came down in glistening, white plates melting at 135°. The compound did not appear to be pure because the melting point was not very sharp, and no concordant analyses could be obtained. Time was lacking for the preparation of larger quantities of this interesting material, but a more complete study of it will be made in the near future.

Secondary Amines with Which no Condensation Compounds Were Formed.

The following acyl derivatives of ortho- and paraminophenol: *Paranitrobenzoylparaminophenol, diparanitrobenzoylparaminophenol, metanitrobenzoylparaminophenol, dimetanitrobenzoylparaminophenol, paranitrobenzoylorthoaminophenol, diparanitrobenzoylorthoaminophenol, metanitrobenzoylorthoaminophenol, dimetanitrobenzoylorthoaminophenol, phenylsulphoneparaminophenol, phenylsulphoneorthoaminophenol, and diphenylsulphoneorthoaminophenol* were heated under pressure, in benzene solution, with camphoroxalic acid to temperatures varying from 165° to 175°, being maintained at these temperatures for several hours, but in no case was there any reaction.

In a paper which we published about a year ago[1] on "Acyl Derivatives of Ortho- and Paraminophenol," we described the preparation and properties of metanitrobenzoylorthoaminophenol and stated that we had prepared it for the first time. Professor Ransom has pointed out to us that he was the first to obtain this compound, as stated in his dissertation.[2]

Paracetoaminophenol was also heated under pressure, in benzene solution, with camphoroxalic acid, at 160°, but no reaction took place.

Benzoylphenylhydrazine and camphoroxalic acid were heated, in benzene solution, at 150° under pressure, and a tarry mass was formed. This was treated with sodium carbonate and the insoluble part dissolved in various solvents, but no definite compound could be isolated. On acidifying the sodium carbonate solution with dilute hydrochloric acid, a small amount of camphoroxalic acid separated.

[1] This Journal, 37, 51 (1907).
[2] Univ. of Chicago, 1900, p. 28.

Benzylphenylhydrazine and camphoroxalic acid were heated in benzene solution, at 140°. A gum formed and this was treated in the same manner as described for the gum from benzoylphenylhydrazine, but no definite compound could be obtained.

Benzylmethylamine and camphoroxalic acid were mixed and heated in absolute ethyl alcohol solution for a short time. The alcohol was then evaporated and a gummy mass was formed, from which no definite compound could be separated.

Phenylmethylhydrazine and camphoroxalic acid were mixed and heated for a short time with absolute methyl alcohol. The solvent was evaporated slowly and a gum was left. This was treated with various solvents but no crystals could be separated from the gum. This latter was then treated with sodium carbonate solution and extracted with ether. The ether solution deposited only a resinous mass, from which no definite compound could be isolated. The sodium carbonate solution was acidified with dilute hydrochloric acid and some camphoroxalic acid separated.

Benzylaniline and camphoroxalic acid were mixed and heated, in benzene solution, for an hour and then the benzene evaporated gradually. A viscid liquid was left, from which no definite compound could be separated. This was then treated with sodium carbonate and extracted with ether. Benzylaniline was left on evaporating the ether, and from the sodium carbonate solution camphoroxalic acid separated on acidifying the liquid with dilute hydrochloric acid.

Phenyl-β-naphthylamine and camphoroxalic acid were heated in benzene solution, under pressure, at 160°, but no reaction whatever took place.

Paraphenylhydrazinesulphonic acid and camphoroxalic acid were heated under pressure, in benzene solution, at 175°, but the two compounds were recovered unchanged.

The action of *benzalaniline* on camphoroxalic acid will be described in a subsequent paper.

Some months after the completion of the work described in the preceding pages, we noticed a paper by O. Dimroth[1]

[1] Ber. d. chem. Ges., 40, 2404 (1907).

on the interaction of *p*-nitrobenzenediazonium hydroxide and certain ketonic and enolic compounds. After a general discussion of the subject, he suggests the following four equations as representing the possible modes of condensation of these substances:

(1) $-\overset{|}{\underset{|}{C}}OCHH + HON:NR \rightarrow -COCHN:NR;$

(2) $HO\overset{|}{\underset{|}{C}}:\overset{|}{\underset{|}{C}}H + HON:NR \rightarrow HO\overset{|}{\underset{|}{C}}:\overset{|}{\underset{|}{C}}N:NR;$

(3) $HO\overset{|}{\underset{|}{C}}:\overset{|}{\underset{|}{C}}OH + HON:NR \rightarrow$

$$H\overset{|}{\underset{|}{C}}:\overset{|}{\underset{|}{C}}ON:NR \rightarrow HO\overset{|}{\underset{|}{C}}:\overset{|}{\underset{|}{C}}N:NR;$$

(4) $HO\overset{|}{\underset{|}{C}}:\overset{|}{\underset{|}{C}}H + HON:NR \rightarrow$

$$(HO)_2\overset{|}{\underset{|}{C}}\overset{|}{\underset{|}{C}}HN:NR \rightarrow HO\overset{|}{\underset{|}{C}}:\overset{|}{\underset{|}{C}}N:NR.$$

The last equation is correct as given here, but is erroneous in Dimroth's paper. Dimroth rejects equation (1) because he failed to obtain condensations with the ketonic compounds which he investigated. The second equation is also discarded because enolic acetyldibenzoylmethane and enolic ethyl diacetylsuccinate, which contain no CH group, condense readily with the diazonium derivative. As between the third and fourth equations, he favors the latter, because only "enols (phenols), but not their ethers or esters, are reactive" in this sense. He states, however, that it is impossible to decide between the two equations until additive compounds of the one or other kind have been prepared and investigated. Dimroth has evidently failed to acquaint himself with the literature on the subject of his investigation, otherwise he would not have overlooked the fact that the senior author alone, and also in conjunction with Alfred Tingle, W. E. Hoffman, Jr., and C. J. Robinson, has described a number of such *addition* compounds, which are termed *camphoformolamine* derivatives, the most interesting being those of camphoroxalic acid with hydroxylamine and *p*-bromphenylhydrazine, respectively. These are, of course, apart altogether from the additive compounds mentioned for the first time in the present communication.

The description of the substances in question, together with full discussions of their constitution and of the bearing which they have on the enolic-ketonic question, are to be found in some eight or ten papers, published at intervals during the past 10 years, chiefly in THIS JOURNAL. The question is dealt with most fully, perhaps, in the paper by Bishop Tingle and Robinson.[1] If Dimroth's reasoning is correect, it follows that the question under consideration was settled some years ago by Bishop Tingle and his colleagues, who regard the fourth of the above equations as the correct representation of the reactions in question, and who have, therefore, always formulated their results in accordance with it. We are glad to receive Dimroth's adhesion to the views which the senior author first recorded many years ago, and although his experimental results are in no way decisive for either method of formulation, yet we welcome them because, in so far as they go, they support the work of the senior author.

The work described in the preceding pages was carried out at the Johns Hopkins University; it will be continued by the senior author at this University.

We desire, in conclusion, to express our grateful thanks to the Trustees of the Warren Research Fund of the American Academy of Arts and Sciences for a grant in aid of the purchase of some of the chemicals employed in this investigation.

MCMASTER UNIVERSITY,
TORONTO, CANADA,
July, 1907.

ON THE AFFINITY CONSTANTS AND CONSTITUTION OF SEVERAL URAZOLES.

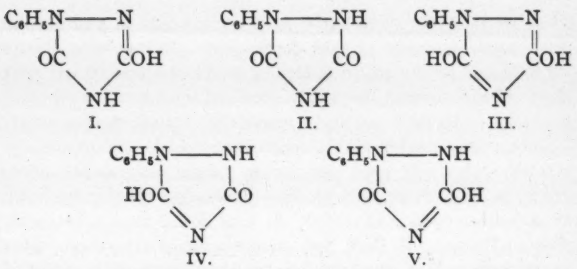
[ELEVENTH COMMUNICATION ON THE URAZOLES.]

BY S. F. ACREE AND G. H. SHADINGER.

Phenylurazole must have one of the five following formulas:[2]

[1] THIS JOURNAL, **36**, 223 (1906).

[2] *Ibid.*, **27**, 118; **31**, 185, **32**, 606; **37**, 71, 361; **38**, 1. Ber. d. chem. Ges., **35**, 553; **36**, 3139; **37**, 184, 618.



It has been proven that it does not exist in solution appreciably as formula V.,[1] and that it seems to react chiefly as formula I. in equilibrium with small amounts of formulas II. and III. and, perhaps, much less of formula IV.

Since both phenylurazole and phenyl-3-thiourazole form salts which, when treated with alkyl halides or alkyl sulphates, are alkylated chiefly in the 2,3 amide group, it seemed probable at the beginning of this investigation that this group is more strongly acid than the 4,5 amide group.

Since, in general, enol groups are stronger acids than keto groups, it seemed probable that the 2,3 group is present in solution largely in the enol form, and the 4,5 group chiefly in the keto form. Corroborative evidence was found in the action of diazomethane upon urazoles, thiourazoles, etc. These reactions showed that the 2,3 amide group of phenylurazole in ether solution is nearly all enol form in equilibrium with a small amount of keto form, while the 4,5 amide group is nearly all keto form in equilibrium with a small amount of enol form. In each case studied, the derivatives of phenylurazole seem to behave in an entirely analogous way.

1-Phenyl-3-thiourazole, however, reacts towards diazomethane in ether solution as if the 2,3 amide group were practically completely enol in structure, and the 4,5 amide group as if it were chiefly keto derivative in equilibrium with a small amount of enol compound.

All of the 1-phenyl-2- or 3-alkylurazoles studied react as if

[1] Ber. d. chem. Ges., **36**, 3139.

they were nearly completely keto compounds in equilibrium with small amounts of enol derivatives. It has been clearly pointed out, however, in a former article by one of us[1] that the evidence secured by purely chemical means or by physical chemical methods is not to be considered entirely trustworthy.

Compounds having a keto structure might be comparatively strong acids, and enol derivatives might be weak acids. It is possible that such elusive tautomeric substances, even though they may exist chiefly as enol form, may react with diazomethane as if they had only the keto structure. This would happen if (1) the keto form reacts more rapidly with the diazomethane than does the enol form, (2) the keto form is in equilibrium with the enol form, and (3) the two forms change into each other very rapidly.

It is perfectly clear, then, that other evidence must be brought to bear on the problem of the constitution of these tautomeric urazoles, and the object of the work presented in this communication was to see what light the application of some of the methods of physical chemistry could throw on the subject.

If this chemical evidence is to be depended upon, a study of the conductivity of these urazoles ought to show that the 2,3 amide group is a very much stronger acid than the 4,5 amide group. The prediction has been fully verified experimentally and the results which were obtained amply confirm the validity of the conclusions drawn from the earlier evidence.

Table A.

Urazoles.	Affinity constants.
1-Phenylurazole	0.000011
1-Phenyl-4-methylurazole	0.000011
1-Phenyl-2-methylurazole	0.000000065
1-Phenyl-3-ethoxyurazole	0.000000043

Table B.

Thiourazoles.	Affinity constants.
1-Phenylthiourazole	0.017
1-Phenyl-4-methylthiourazole	0.017
1-Phenyl-3-ethylthiourazole	0.00000075
1-Phenyl-3-methylthiourazole	0.00000020

[1] Acree: THIS JOURNAL, 38, 1.

In Table A. above, it is seen that the affinity constants of phenylurazole and phenyl-4-methylurazole are practically the same. This proves that, as was anticipated, most of the hydrogen and urazole ions of phenylurazole come from the 2,3 enol group and very little from the 4,5 keto group. It was, therefore, predicted that when the 2,3 amide hydrogen is replaced by a radical the affinity constant would fall to a marked extent. This idea has been amply verified, especially when hydrogen is replaced by methyl in the 2 position or by ethyl in the 3 position, the value for the affinity constants falling to about one-half of one per cent of that for phenylurazole. The methyl and ethyl radicals have about the same influence upon the 4,5 amide group.

In Table B. similar results are shown for the thiourazoles. Again the 1-phenyl-4-methyl-3-thiourazole has practically the same affinity constant as the phenyl-3-thiourazole itself. This proves that most of the hydrogen ions come from the 2,3 enol group and that the 4,5 amide (keto) group is a very weak acid. When the hydrogen of the 2,3 amide group of phenyl-3-thiourazole is replaced by the methyl or ethyl radical a marked diminution in strength is shown by the alkylurazole formed. Both radicals affect the affinity constant of the 4,5 amide group to about the same degree, as was the case with phenylurazole. It is interesting to note that by a replacement of the 3-ethoxy and 2-methyl groups by the more negative 3-thioethyl and 3-thiomethyl groups, the affinity constants become from 4 to 15 times as large.

Previous chemical work had led to the conclusion that phenyl-3-thiourazole is a much stronger acid than phenylurazole. Phenyl-3-thiourazole titrates more sharply with alkalis than does the phenylurazole and it is strong enough to color methyl orange red, whereas phenylurazole does not. A comparison of Tables A. and B. shows that the 1-phenyl-3-thiourazole and 1-phenyl-4-methyl-3-thiourazole are 1500 times as strong as the phenylurazole and 1-phenyl-4-methylurazole. This confirmation of the purely chemical evidence by that secured by the use of physical chemical methods is very satisfactory. In order to secure conclusive evidence

regarding the constitution and reaction of such tautomeric compounds both methods must be used.

During the time required to read the conductivity of these compounds there seemed to be no tautomeric changes, but, as the writers had already observed while studying certain alkylation reactions by means of titration methods, there was a change of phenyl-3-thiourazole and phenyl-4-methyl-3-thiourazole into the disulphides. See Tables 10 and 12 in Section I., and Table 36 in Section II., in the next article by the writers.

Conductivity Apparatus.

The Kohlrausch method of measuring conductivity with a Wheatstone bridge, a telephone receiver, and an induction coil, was used. The bridge wire was made of "manganin" and was carefully calibrated. The resistance coils were standardized and found to be accurate to 0.04 per cent.

The conductivity cells were of the form used by Jones and Bingham.[1] These cells contained no material soluble in the solvent, prevented evaporation, and protected anhydrous solvents from the moisture of the atmosphere.

The electrodes were coated with platinum black, and then heated in a blast lamp until they became white. This white coating neither absorbs salts nor exerts any oxidizing action.

The sliding contact for determining the zero point was of a special form, as illustrated in Fig. I.,

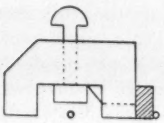


Fig 1 End View

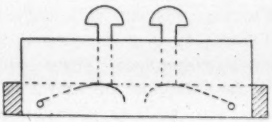


Fig 1, Side View

having a double contact. The two buttons are pressed down alternately. This can be done quickly, and in this way a much more accurate reading can be made in a shorter time, as the

[1] This Journal, **36**, 493.

error involved in having to remember the sound is much less than when the ordinary single contact is used.

Solvents.

Water.—The water was purified by the method of Jones and Mackay[1] and had a conductivity of from 1.8 to 2.3×10^{-6} at 25°.

Ethyl Alcohol.—The best commercial article was digested with calcium oxide and distilled through a Linnemann fractionating head. The conductivity was 2×10^{-6} at 25°.

Standard Alcoholic Hydrochloric Acid.—The alcohol prepared as above was put into a graduated flask and dry hydrochloric acid gas passed in until a slight excess over the weight required for the standard solution was obtained. The flask was filled to the mark with alcohol and the calculated amount necessary to make the solution of standard strength was then added.[2]

Bath.

The 25° bath was of the usual form, the stirrer being driven by a water motor. An Ostwald regulator was employed, but the gas channel was constricted enough to make the apparatus sensitive to 0.01°. The thermometer was standardized and graduated into tenths of a degree, but could be read easily to within 0.01°. Solutions of the urazoles in water were always made as concentrated as possible and then dilutions made as far as it was practicable to measure the conductivities.

Conductivity Measurements.

In all determinations at least three different resistances were used and the values given are the mean. The constants of the cells were checked at frequent intervals. When not in use, the cells were filled with pure water. A 0.02 normal solution of potassium chloride was used in determining the cell constants. The conductivity of the 0.02 normal solution was taken as 129.7 at 25°. All work was done at 25°.

The μ_∞ of the Sodium Salts and of the Urazole Acids.—The $\mu\infty$ of each sodium urazole was obtained by diluting the solutions until a maximum molecular conductivity was reached. Since

[1] This Journal, **19**, 91.

[2] Acree and Brunel: *Ibid.*, **38**, 117.

the sodium salts of the urazole acid esters are hydrolyzed in dilute solutions, enough of the acid ester itself was added to the solution to suppress this hydrolysis. The conductivity of the urazole acid ester in the presence of its salt is small enough to be neglected, as can be seen from Table 6.

The μ_∞ of the acids and acid esters was obtained by the use of Kohlrausch's law. This value was, on the average, about 355, which is about the same as that for other acids having nearly the same molecular weight.

The affinity constants of the urazoles were then obtained by using Ostwald's formula for the acids and acid esters and Rudolphi's formula for the sodium salts. It was shown in a former article by one[1] of us that the formula

$$\frac{H \times (C_{ki} + C_{ei})}{(C_k + C_e)} = \frac{(K_2 + K_1K_3)}{(1 + K_3)} = K$$

gives the correct affinity constant for such tautomeric urazole acids. H is the concentration, in gram molecules per liter, of the hydrogen ions, C_{ki} that of the keto anions, C_{ei} that of the enol anions, C_k that of the keto molecular form, C_e that of the enol molecular form, K_1 the affinity constant of the keto tautomer, K_2 that of the enol tautomer, and K_3 the ratio of the amount of keto molecular form to that of the enol molecular form. Since the ionic velocities of the enol and keto anions are approximately the same, the above equation assumes the form of the one used by Ostwald,

$$\frac{\alpha^2}{1 - \alpha} = \frac{\mu^2 v}{\mu_\infty (\mu_\infty - \mu_v)} = KV.$$

The same reasoning shows that the Rudolphi dilution equation holds for the salts of tautomeric acids or bases.

EXPERIMENTAL.

Phenylurazole.—This was made by the method of Acree.[2] One hundred grams of phenylhydrazine gave 100 grams of phenylurazole which, after recrystallization from alcohol, melted at 265° to 267° without decomposition. This was crystallized

[1] Acree: THIS JOURNAL, **38**, 12.
[2] *Ibid.*, **27**, 126.

twice from alcohol, and water solutions were made for the conductivity measurements.

Sodium Salt of Phenylurazole.—Fifteen grams of the pure phenylurazole were heated for several hours in conductivity water in a beaker with the theoretical weight of sodium bicarbonate. Upon evaporating the solution to a small volume and cooling it, a white precipitate was formed. This was crystallized three times from distilled water and twice from conductivity water and dried in a desiccator over sulphuric acid.

The following method of analysis was followed for all sodium salts: About 0.3 gram was weighed into a platinum crucible and 3 cc. dilute sulphuric acid were added. This mixture was evaporated and the residue was ignited in a Rogers burner; the process was then repeated and the product was weighed as sodium sulphate.

Analysis:

0.2519 gram anhydrous substance gave 0.0869 gram Na_2SO_4.

6.6233 gram substance lost 1.1528 gram H_2O at 120°.

	Calculated for $C_8H_6O_3N_2Na$.	Found.
Na	11.54	11.17

	Calculated for $C_8H_6O_3N_2Na.2H_2O$.	Found.
$2H_2O$	17.25	17.40

Table I.—Sodium 1-Phenylurazole. $\mu_\infty = 80.44$.

V.	μ_v.	α.	$K = \frac{\alpha^2}{(1-\alpha)\sqrt{v}}$.
16	57.77	0.719	0.447
32	60.04	0.747	0.388
64	62.40	0.775	0.335
128	65.05	0.809	0.302
256	67.72	0.841	0.280
512	70.00	0.870	0.258
1024	81.58	1.014	
2048	79.28	0.985	

The maximum molecular conductivity of the acid is obtained as follows: By the law of Kohlrausch $C+A = 80.44$ for the sodium salt; therefore $A = 80.44 - 49.2 = 31.24$, and the $\mu\infty$ of the acid is $31.24+325$ or 356.24.

Table II.—1-Phenylurazole. $\mu_\infty = 356.24$.

V.	μ_v.	α.	$K = \frac{\alpha^2}{(1-\alpha)}v$.
512	26.36	0.0740	0.0000115
1024	36.30	0.102	0.0000118
2048	47.77	0.134	0.0000102
4096	65.38	0.183	0.00000984
8192	82.25	0.230	0.00000946
16384	125.55	0.352	0.0000121
			$K = 0.000011$

Sodium Salt of 1-Phenyl-2-methylurazole.—Two grams of phenyl-2-methylurazole in water were treated with the theoretical weight of pure sodium bicarbonate and heated some hours in a beaker to expel the carbon dioxide. When the solution was evaporated to a small volume and cooled, the salt precipitated out. It was recrystallized three times from conductivity water.

Analysis:

0.2745 gram of anhydrous substance gave 0.1005 gram Na_2SO_4.

0.7227 gram substance gave 0.1445 gram H_2O at 120°.

	Calculated for $C_9H_8O_2N_2Na$.	Found.
Na	10.79	10.85
	Calculated for $C_9H_8O_2N_2Na.3H_2O$.	Found.
$3H_2O$	20.20	19.99

Table III.—Sodium 1-Phenyl-2-methylurazole. $\mu_\infty = 69.2$.

V.	μ_v.	α.	$K = \frac{\alpha^2}{(1-\alpha)\sqrt{v}}$.
64	59.07	0.8576	0.622
128	61.26	0.885	0.603
256	62.76	0.907	0.552
512	64.37	0.930	0.548
1024	66.10	0.955	0.637
2048	71.52	1.033	
Hydrolysis suppressed with molecular amount of 1-phenyl-2-methylurazole.			
2048	69.255	1.000	

The maximum molecular conductivity of the acid is obtained as follows: $C+A = 69.2$ for the sodium salt; therefore, $A = 69.2 - 49.2 = 20$, and the μ_∞ of the acid is $20+325$ or 345.

1-Phenyl-2-methylurazole.[1]—Twenty-four grams of phenylurazole were dissolved in a small amount of water containing one molecular proportion of sodium hydroxide. Two molecules of dimethyl sulphate, which had been shaken with alkali to remove the free acid, were added and the whole shaken one-half hour. The precipitate was recrystallized three times from distilled water, hydrolyzed with hydrochloric acid to decompose any methoxy derivative, extracted with chloroform to remove the phenylurazole, and recrystallized from conductivity water. Four grams of pure product were obtained which melted at 185°.

Table IV.—1-Phenyl-2-methylurazole. $\mu_\infty = 345$.

V.	μ_v.	α.	$K = \frac{\alpha^2}{(1-\alpha)V}$
128	1.007	0.00291	0.0000000668
256	1.452	0.00420	0.0000000694
512	1.849	0.00535	0.0000000564
1024	2.527	0.00732	0.0000000664
2048	6.894	0.0199	(0.000000197)
4096	8.155	0.0237	(0.000000140)

$K = 0.000000065$

Sodium Salt of 1-Phenyl-3-ethoxyuzazole.—This was prepared and purified in a manner similar to that employed for the preparation of the sodium salts spoken of above.

Analysis:

0.2999 gram of anhydrous substance gave 0.0883 gram Na_2SO_4.

	Calculated for $C_{10}H_{10}O_3N_2Na$.	Found.
Na	10.12	10.70

[1] For a description of the derivatives of phenylurazole used in this work, see the article by Acree: THIS JOURNAL, 38, 1.

Table VI.—Sodium 1-Phenyl-3-ethoxyurazole. $\mu_\infty = 82$.

V.	μ_v.	α.	$K = \frac{\alpha^2}{(1-\alpha)\sqrt{V}}$.
32	59.13	0.721	0.329
64	61.96	0.755	0.292
128	64.25	0.783	0.250
256	65.22	0.795	0.193
512	67.33	0.821	0.200
1024	69.72	0.850	0.150
4096	77.18	0.941	0.235
Suppression of hydrolysis by an equal amount of 1-phenyl-3-ethoxyurazole.			
4096	82.14	1.001	
8192	81.62	0.995	

The maximum molecular conductivity of the acid is obtained as follows: $C + A = 82$ for the sodium salt; therefore $A = 82 - 49.2 = 32.8$, and the μ_∞ of the acid is $32.8 + 325$ or 357.8.

1-Phenyl-3-ethoxyurazole.—Much difficulty was experienced in obtaining this ester in large quantities by the alkylation of phenylurazole salts, and several methods were tried before a satisfactory one was found.

1. Alkylation Experiments in Ether as a Solvent.—Seventy-five grams of phenylurazole and a drop of phenolphthalein solution were titrated with a solution of potassium hydroxide. The solution was warmed and one molecular portion of silver nitrate in a little water was added with constant stirring. The silver salt was white when first formed, but soon turned dark. When washed with alcohol and ether and dried, it weighed 112 grams. Forty-five grams of this silver salt, suspended in 400 cc. of ether, and 1.5 molecules of ethyl iodide (37.5 grams) were boiled two days in a liter flask under a return condenser. The silver residue was filtered off and the ether filtrate was treated in the cold with a slight excess of dilute potassium hydroxide solution to extract the 1-phenyl-3-ethoxyurazole. This alkaline extract, when acidified with dilute sulphuric acid, gave a white precipitate of phenylurazole, 1-phenyl-3-ethoxyurazole, 1-phenyl-2-ethylurazole, and perhaps other products, and more of the ethyl esters were obtained by extracting the filtrate with ether or chloroform. Recrystal-

lization of the precipitate from a large amount of 50 per cent alcohol gave pure white, needlelike crystals which melted from 150° to 200°. When this precipitate was treated with chloroform and filtered, a small quantity of phenylurazole was left as an insoluble residue. The chloroform filtrate was evaporated and the residue was crystallized from 50 per cent alcohol. Crystals of pure 1-phenyl-3-ethoxyurazole were obtained which melted at 152° and weighed 1.2 grams. The filtrate from the 1-phenyl-3-ethoxyurazole was evaporated and it then gave 1.8 grams of crystals melting at 75° to 80°, which were probably largely 1-phenyl-2-ethylurazole. The ether solution from which the 1-phenyl-3-ethoxyurazole and 1-phenyl-2-ethylurazole were extracted retained the 1-phenyl-3,5-diethoxyurazole. The ether was evaporated off and a yellow oil was obtained which solidified on standing. This oil weighed 3.2 grams. When it was dissolved in alcohol and water was added, fine white needles were precipitated. The 1-phenyl-3,5-diethoxyurazole, when crystallized twice, as before, melted at 52°. The yield was 2.5 grams. This method was repeated twice and in both cases the same poor yields were obtained.

2. *Shaking the Silver Salt and Ethyl Iodide in Cold Ether.*—The same quantities of reagents were used as in the preceding experiment, but were shaken in a stoppered bottle three days. When the reaction product was treated as before the yield was 1.4 grams of 1-phenyl-3-ethoxyurazole (melting point 147° to 149°), 2.2 grams of low melting product (melting point 68° to 74°), and 3.6 grams of crude 1-phenyl-3,5-diethoxyurazole.

3. *Silver Phenylurazole and Pure Ethyl Iodide in the Cold.*—Ten grams of silver salt were shaken four days in a bottle with 50 grams of ethyl iodide. When the reaction product was treated as before, the yield was 0.1 gram 1-phenyl-3-ethoxyurazole, 0.5 gram low melting material (melting point 68° to 76°), and 0.7 gram crude 1-phenyl-3,5-diethoxyurazole. The yields for these three methods are about the same.

4. *Silver Phenylurazole and Pure Ethyl Iodide in Sealed Tubes.*—Fifty grams of the silver salt were put in two large Carius tubes and enough ethyl iodide (320 grams) was added to make a soft

mush. The tubes were heated two days at 50° and two days at 75°. When the reaction product was treated as before it gave 4 grams of 1-phenyl-3,5-diethoxyurazole in good condition, although it had to be crystallized first from pure alcohol. The fraction which should have been 1-phenyl-3-ethoxyurazole contained so little of this that it could not be separated from the 1-phenyl-2-ethylurazole by the ordinary methods. This fraction melted at 65° to 85°.

5. *Silver Phenylurazole and Ethyl Iodide in Ether in Sealed Tubes.*—Seventy-five grams of the silver salt were put into two tubes with two molecular proportions of ethyl iodide, and three or four times the volume of ether was then added. These two tubes were heated three days at 75°, when an accident caused the loss of one tube. The contents of the other were treated as before and gave 4 grams of 1-phenyl-3,5-diethoxyurazole in good condition, but the other product melted low, as before. This low melting material was titrated with 55 cc. of 0.1 normal sodium hydroxide solution and the urazoles were fractionally precipitated with 0.1 normal sulphuric acid. Eleven cc. of acid were used for each fraction. The first precipitate melted at 100° to 150°; the second at 80° to 125°; the third, fourth, and fifth at 72° to 95°. The first fractions were recrystallized three times from alcohol and gave 2 grams of 1-phenyl-3-ethoxyurazole, which melted at 151° to 152°. This last method seems the best of the five given.

The unchanged phenylurazole left with the silver residue can be recovered by saturating the required amount of potassium hydroxide solution with hydrogen sulphide and digesting the silver salt with the solution in the cold several hours. When the silver sulphide is filtered off and the filtrate is boiled to remove hydrogen sulphide, and acidified, the phenylurazole precipitates out in pure condition.

6. *Preparation and Hydrolysis of 1-Phenyl-3,5-diethoxyurazole.*—Thirty grams of phenylurazole were converted into disilver phenylurazole[1] by dissolving the phenylurazole in somewhat more than one molecular proportion of potassium hy-

[1] Acree: THIS JOURNAL, **38**, 1; Ber. d. chem. Ges., **38**, 3146.

droxide solution, then adding nearly one molecular proportion of silver nitrate in solution, and then, alternately, solutions of potassium hydroxide and silver nitrate in separate portions until two molecular proportions of each had been used. The silver salt was prepared in a two-liter bottle which was shaken violently during the experiment. Only small quantities of the reagents should be added each time, and the bottle must be shaken *well* after each addition. The bottle was then agitated for several hours in a machine. After standing overnight, the gelatinous material was collected so that it could be filtered. It was dried in the air on porous plates. Heating, to hasten drying causes decomposition. The yield is always quantitative. The salt was then put in a flask with 500 cc. of ether and three molecular proportions of ethyl iodide and boiled three days. After filtering off the silver salts, the filtrate was extracted with potassium hydroxide solution. When the alkaline solution was acidified, it gave 1.2 grams of yellowish crystals melting at 66° to 73°.

After the ether was distilled off, the yellow oil which was left solidified. After crystallizing this solid from 95 per cent alcohol, 9.5 grams of 1-phenyl-3,5-diethoxyurazole were obtained, which melted at 52° to 53°. From the filtrate 5.2 grams of the same compound melting at 49° to 52° were obtained. It was found that, when the pure 1-phenyl-3,5-diethoxyurazole was heated in a sealed tube one hour at 85° with exactly one molecular proportion of hydrogen chloride in alcohol, the 5-ethoxy group was hydrolyzed quantitatively and pure 1-phenyl-3-ethoxyurazole was left. When the impure fraction, melting at 49° to 52°, was hydrolyzed with alcoholic hydrochloric acid, it gave 1-phenyl-3-ethoxyurazole which, after crystallization from 50 per cent alcohol, melted at 150° to 151°. This last method is the most satisfactory one used for the preparation of 1-phenyl-3-ethoxyurazole.

The sample of 1-phenyl-3-ethoxyurazole used in the conductivity measurements was recrystallized several times from pure 50 per cent alcohol.

Table VII.—1-Phenyl-3-ethoxyurazole.

$\mu_\infty = 357.8$.

V.	μ_v.	α.	$K=\frac{\alpha^2}{(1-\alpha)V}$
1024	2.106	0.00589	0.0000000340
2048	3.470	0.00961	0.0000000463
4096	4.451	0.0124	0.0000000382
8192	7.072	0.0198	0.0000000487

$K = 0.000000043$

1-Phenyl-4-methylurazole.—This was made by the hydrolysis of 1-phenyl-3-ethoxy-4-methylurazole with hydrochloric acid.[1] This latter ester was made by treating 8 grams of 1-phenyl-3-ethoxyurazole with one molecular proportion of potassium hydroxide in 50 cc. of water and shaking the solution one hour with 1.5 molecular proportions of neutral dimethyl sulphate. Potassium hydroxide in solution was added from time to time to keep the solution alkaline. The product soon crystallized out. It was found that the yield is always much better if the solution is warmed before shaking. When recrystallized three times from alcohol containing a small amount of potassium hydroxide, the 1-phenyl-4-methyl-3-ethoxyurazole melted at 96°. Four grams of this ester were evaporated three times with concentrated hydrochloric acid and the residue was crystallized from alcohol. Three grams of 1-phenyl-4-methylurazole, melting at 225°, were obtained.

Table VIII.—1-Phenyl-4-methylurazole.

$\mu_\infty = 355$.

V.	μ_v.	α.	$K=\frac{\alpha^2}{(1-\alpha)V}$
512	26.98	0.076	0.0000122
1024	37.49	0.105	0.0000121
2048	46.76	0.132	0.0000136
4096	61.94	0.174	0.00000900
8192	74.67	0.210	(0.00000683)

$K=0.000011$

Sodium Salt of 1-Phenyl-4-methylurazole.—This salt was made by the method used for preparing the other sodium salts.

[1] Acree: THIS JOURNAL, 38, 1.

Table IX.—Sodium Salt of 1-Phenyl-4-methylurazole.

$\mu_\infty = 82.81$.

V.	μ_v.	α.	$K=\frac{\alpha^2}{(1-\alpha)\sqrt{V}}$.
64	55.80	0.674	0.174
128	62.19	0.751	0.200
Hydrolysis suppressed with 0.25 molecule of 1-phenyl-4-methylurazole.			
256	61.17	0.739	0.130
512	63.99	0.773	0.116
1024	63.80	0.770	0 0808
2048	68.07	0.822	0.0839
4096	71.37	0.862	0.0594
8192	82.81	1.00	

1-Phenyl-3-thiourazole.—This was made by Acree's method.[1] Ethyl 1-phenylthiosemicarbazide-1-carboxylate was extracted in a Soxhlet apparatus with alcohol and consequently the phenyl-3-thiourazole was obtained in excellent condition. For further purification it was dissolved in an excess of potassium hydroxide, heated two hours, and again precipitated by the addition of hydrochloric acid. When it was recrystallized twice from alcohol, it melted at 192° to 193°. The μ_∞ for all of the thiourazoles used in this work was assumed to be 355, which is certainly not far from the correct value. An error of even 10 conductivity units makes no appreciable error in the values of the affinity constants.

Table X.—1-Phenyl-3-thiourazole.

$\mu_\infty = 355$.

V.	μ_v.	α.	$K=\frac{\alpha^2}{(1-\alpha)V}$.
64	226.41	0.637	0.0175
128	271.68	0.765	0.0194
256	292.78	0.824	0.0151
Disulphide was formed very rapidly.			
512	305.96	0.861	(0.0105)
1024	295.43	0.822	(0.00403)
2048	143.30	0.403	
			$K=0.017$

[1] Ber. d. chem. Ges., 36, 3151.

Sodium Salt of 1-Phenyl-3-thiourazole.—This salt was made by dissolving the theoretical weight of pure sodium bicarbonate in water, adding the 1-phenyl-3-thiourazole, and boiling the solution to expel the carbon dioxide. The solution was evaporated to dryness and the residue was heated two hours in an air bath. At the end of this time, all water of crystallization had been driven off and the weight was constant.

Table XI.—Sodium Salt of 1-Phenyl-3-thiourazole.

$\mu\infty = 77.35$.

V.	μ_v.	α.	$K = \frac{\alpha^2}{(1-\alpha)\sqrt{V}}$
16	41.09	0.501	0.126
32	43.03	0.525	0.129
64	44.62	0.570	0.0946
128	49.09	0.599	0.0791
256	48.19	0.588	0.0525
512	50.78	0.619	0.0446
1024	64.95	0.728	0.0948
2048	58.96	0 719	0.0408
4096	67.72	0.826	0.0445
8192	77.35	1.00	

1-Phenyl-4-methyl-3-thiourazole.—This urazole derivative was made by the method suggested by Acree.[1] The 1-phenyl-4-methylthiosemicarbazide was made from phenylhydrazine and methyl mustard oil.[2] The ethyl 1-phenyl-4-methylthiosemicarbazide-1-carboxylate was made from 1-phenyl-4-methylthiosemicarbazide and ethylchlorcarbonate by Acree's method.

The reagents for making the ester were dissolved in chloroform and the solution was heated one day. When the reaction mixture was cooled, the ester which crystallized out melted at 196°. The chloroform was distilled off and the residue solidified. At first it melted slightly under 100°, but when recrystallized twice from alcohol, its melting point was 102° to 103°. This substance was not identified.

[1] Acree: Ber. d. chem. Ges., **36**, 3154.

[2] Dixon: J. Chem. Soc., **87**, 261. Busch: Ber. d. chem. Ges., **37**, 2332. Marckwald: *Ibid.*, **25**, 3107.

Table XII.—1-Phenyl-4-methyl-3-thiourazole.

$\mu\infty = 355$.

V.	μ_v.	α.	$K = \frac{\alpha^2}{(1-\alpha)V}$
256	299.72	0.844	0.0178
512	309.66	0.872	0.0116
Disulphide was formed very rapidly.			
1024	269.18	0.758	(0.00232)
2048	283.18	0.797	(0.00146)
4096	281.49	0.792	(0.000741)
8192	292.56	0.823	(0.000471)

$K = 0.017$

1-Phenyl-3-methylthiourazole.[1]—Five grams of phenylthiourazole were neutralized with normal potassium hydroxide solution. This solution was diluted with two-thirds of its volume of alcohol and 1.15 molecular proportions of methyl iodide, and was then boiled fifteen minutes. The new material crystallized out when the solution was cooled. This ester was purified by crystallizing it from water, from alcohol containing a little methyl iodide, from absolute alcohol, and then from conductivity water. It weighed 3.5 grams and melted at 174° to 175°.

Table XIII.—1-Phenyl-3-methylthiourazole.

$\mu\infty = 355$.

V.	μ_v.	α.	$K = \frac{\alpha^2}{(1-\alpha)V}$
1024	4.02	0.0113	0.000000126
2048	5.37	0.0151	0.000000113
4096	10.06	0.0283	0.000000202
16384	25.07	0.0706	0.000000327

$K = 0.0000002$

Sodium Salt of 1-Phenyl-3-methylthiourazole.—This was made and treated like the preceding sodium salts.

[1] Acree: Ber. d. chem. Ges., **36**, 3151.

Table XIV.—Sodium Salt of 1-Phenyl-3-methylthiourazole.

$\mu_\infty = 86.95$.

V.	μ_v.	α.	$K=\frac{\alpha^2}{(1-\alpha)\sqrt{V}}$.
64	63.63	0.731	0.249
128	76.29	0.815	0.318
256	69.07	0.794	0.191
512	73.54	0.845	0.205
1024	72.92	0.838	0.136
2048	82.04	0.943	0.348
4096	84.61	0.973	0.388
8192	86.95	.....	.....

1-Phenyl-3-ethylthiourazole.[1]—The method of preparation and purification was entirely similar to that given for 1-phenyl-3-methylthiourazole. Four grams of pure ester, melting at 137° to 138°, were obtained from 5 grams of phenylthiourazole.

Table XV.—1-Phenyl-3-ethylthiourazole.

$\mu_\infty = 355$.

V.	μ_v.	α.	$K=\frac{\alpha^2}{(1-\alpha)V}$.
2048	10.98	0.0309	0.000000483
4096	19.29	0.0943	0.000000762
16384	42.54	0.119	0.000000996
			$K = 0.00000075$

Barium Salt of 1-Phenyl-3-thiourazole.—This was made by titrating 2 grams of the 1-phenyl-3-thiourazole with the theoretical amount of standard barium hydroxide solution, evaporating the solution and drying the salt as before.

[1] Acree: Ber. d. chem. Ges., 36, 3151.

Table XVI.—Barium Salt of 1-Phenyl-3-thiourazole.

$\mu_\infty = 103.19$.

V.	μ_v.	α.	$=\chi\frac{\alpha^2}{(1-\alpha)\sqrt{V}}$
64	77.04	0.746	0.274
128	87.98	0.852	0.435
256	88.52	0.857	0.323
512	93.89	0.909	0.406
1024	94.54	0.916	0.313
2048	99.80	0.935	0.318
4096	101.18	0.961	0.275
8192	103.19	....	....

1-Phenyl-3-ethoxy-4-methylurazole.—See page 138, under 1-phenyl-4-methylurazole.

On the Basic Properties of Some Urazole Esters.

In order to see if some of the urazole esters are weak bases and unite to some extent with hydrochloric acid in alcoholic solutions,[1] some conductivity measurements were made on alcoholic hydrochloric acid solutions to which varying amounts of the ester were added.

The conductivity of 0.1 normal alcoholic hydrochloric acid at 25° was found to be 21.221.[2] The data available show that the conductivity in absolute alcohol at infinite dilution of a salt having the molecular weight of those probably formed in the experiments below referred to is from one-third to one-fourth that of hydrochloric acid in equal concentration in alcohol. Therefore, the conductivity of the hydrochloride of the 1-phenyl-3-ethoxyurazole and of the other esters was taken to be one-fourth that of the 0.1 normal hydrochloric acid, or 5.302.

The total lowering of conductivity which could be produced if all the base were changed to hydrochloride would then be 21.211 — 5.302 = 15.909. The percentage of salt formed as successive amounts of base were added is found by dividing the lowering in conductivity produced by the total lowering

[1] Acree and Johnson: THIS JOURNAL, **28**, 336.

[2] Wildermann: Z. physik. Chem., **14**, 231, 247. Scholl: *Ibid.*, **14**, 701. Sill: *Ibid.*, **81**, 595. Walden: *Ibid.*, **84**, 129. Godlewski: J. Chim. Phys., **3**, 393.

possible. The data do not take into consideration the small change in volume produced by adding the urazole ester. If the data were sufficiently accurate, the affinity constants of the bases could be calculated.

Table XVII.—1-Phenyl-3-ethoxyurazole in 0.1 N Alcoholic HCl.

Amount of ester added to 25 cc. 0.1 N alcoholic HCl.	μ_v.	Per cent of salt formed.
0 molecule	21.22	....
0.25 "	20.83	3.74
0.50 "	20.50	4.44
0.75 "	20.13	6.76
1.00 "	19.81	8.77
1.25 "	19.42	11.26
1.50 "	19.19	12.69
1.75 "	18.88	15.24
2.00 "	18.47	17.15

Table XVIII.—1-Phenyl-3,5-diethoxyurazole in 0.1 N Alcoholic HCl.

Amount of ester added to 25 cc. alcoholic HCl.	μ_v.	Per cent of salt formed.
0.25 molecule	20.82	2.46
0.50 "	20.46	4.71
0.75 "	20.13	6.75
1.00 "	19.81	8.77
2.00 "	18.39	17.69
3.00 "	17.24	24.94
4.00 "	16.15	31.78

Table XIX .—1-Phenyl-3-ethoxy-4-methylurazole in 0.1 N Alcoholic HCl.

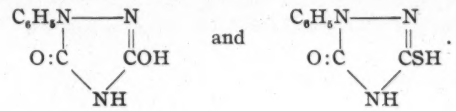
Amount of ester added to 25 cc. alcoholic HCl.	μ_v.	Per cent of salt formed.
0.25 molecule	21.04	1.04
0.50 "	20.74	2.92
1.00 "	20.13	6.75
2.00 "	19.01	13.79

Conclusions.

The affinity constant of the 2,3 amide group of phenylurazole and of 1-phenyl-4-methylurazole is 0.000011, while

that of 1-phenyl-3-thiourazole and 1-phenyl-4-methyl-3-thiourazole is about 1500 times as great, or 0.017. The affinity constant of the 4,5 amide group of the 2-alkyl and 3-alkoxy derivatives of phenylurazole is about 0.00000005, whereas the corresponding derivatives of 1-phenyl-3-thiourazole are several times as strong.

It has therefore been shown by the use of physical chemical and organic methods that those urazoles which seem to have the enol structure have much larger affinity constants than those urazoles which are apparently keto compounds. New evidence has thus been produced in favor of the view that phenylurazole and phenyl-3-thiourazole are tautomeric compounds which exist in solution chiefly in the two forms represented by the formulas



JOHNS HOPKINS UNIVERSITY,
June 10, 1907.

A REPLY TO JULIUS STIEGLITZ'S "NOTE[1] ON THE ARTICLE ENTITLED 'STUDIES IN CATALYSIS'[2] BY S. F. ACREE."

BY S. F. ACREE.

So many of the statements in Mr. Stieglitz's note are at variance with the facts, as I see them, that I feel it to be my duty to myself and to some of my colleagues to present the following statement "in the interest of the question of priority and of historical truth."

In answer to Mr. Stieglitz's statement that (p. 744) "In my address.....the leading ideas of the theory of catalysis, as now put forth again by Acree without due acknowledgment, were already presented," and that (p. 745) "there is not one single new principle presented in Acree's paper,"

[1] THIS JOURNAL, 38, 743.
[2] Acree and Johnson: *Ibid.*, 38, 258.

I shall discuss historically the work of various chemists and *their leading ideas* of the following three fundamental principles believed, until recent years, to apply to catalysis:

(1) The catalyzer seems to act by its simple presence.

(2) The catalyzer affects the velocity constant directly in proportion to the concentration of the catalyzer.

(3) A change in the concentration of the catalyzer does not change the equilibrium point in reversible reactions.

(A) Mr. Stieglitz says (p. 744): "In that address, the first vital and decisive step was taken to depart from the old idea that....the catalytic agent must appear to act by its presence simply and not to form a compound in any quantity with any of the components. '....The most fundamental fact concerning acids was recalled, the fact that they have the power to form *salts* with bases and oxides. ....' We.....could *prove our point that the acceleration is.....due to salt and ion formation.*"

I wish to point out now that every one of these fundamental assumptions, AND ESPECIALLY STIEGLITZ'S KEYNOTE, ACCELERATION THROUGH SALT AND ION FORMATION, *had already been made by Kastle,*[1] *Euler,*[2] *Acree,*[3] *Bredig,*[4] *and Lapworth,*[5] *and that Stieglitz advanced them again as his own without once stating that his ideas were not new. Acree and Johnson gave full credit*[6] *to all of these colleagues and to Stieglitz for their ideas and work. Furthermore, the discovery that the second and third laws of catalysis do not hold in all catalytic reactions was first worked out theoretically by myself and experimentally by Johnson, and also independently by Abel*[7] *and Euler,*[8] *and was not even hinted at or discussed in any phase by Stieglitz.*

(1) In their article on Catalysis, J. H. Kastle and J. C. W.

[1] THIS JOURNAL, **19**, 894. P. Am. Assn. Adv. Sci., **47**, 238. Professor Kastle kindly sent me his original manuscript, from which I give quotations.

[2] Z. physik. Chem., **36**, 405, 663; **40**, 501; **47**, 356. Z. physiol. Chem., **52**, 146.

[3] Acree and Hinkins: THIS JOURNAL, **28**, 370.

[4] Z. Elek. Chem., **9**, 118; **10**, 586; **11**, 528.

[5] See Mellor's Statics and Dynamics, pp. 289, 335, 338, 339, 342.

[6] Acree and Johnson: THIS JOURNAL, **38**, 299, 300, 301.

[7] Z. Elek. Chem., **13**, 555.

[8] Z. physiol. Chem., **52**, 146.

Frazer presented the following views "as the result of our studies on the hydrolysis of sulphonic esters especially":

"First, that the catalytic changes involved in etherification, the hydrolysis of ethereal and metallic salts and acid amides, and the inversion of cane sugar and the similar compounds by acids, are essentially the same in kind.

"Secondly, That hydrolysis and etherification are always preceded by the formation of an unstable addition product (Kastle's salt) of the substance undergoing the catalysis and the acid causing the same; and that it is the decomposition of this unstable addition product by water or alcohol that gives the ultimate products of the catalysis.

"Thirdly, That this unstable addition product is produced by the combination of the ions of the acid causing the catalysis with the anhydride or oxide-like oxygen or element of the compound undergoing the change.

"This hypothesis necessarily involves the idea of the quadrivalence of the oxygen atom."

Kastle represented the formation of the ester from acetic acid, alcohol, and hydrochloric acid, as taking place as indicated below:

$$CH_3COOH + HCl \rightarrow CH_3C(H)(Cl)O{-}OC_2H_5 \rightarrow$$

$$CH_3C(H)O{-}OC_2H_5 + HCl \rightarrow CH_3COOC_2H_5 + H_2O + HCl.$$

For the hydrolysis of ethyl acetate he gave these expressions:

$$CH_3COOC_2H_5 + HCl \rightarrow CH_3C(Cl)(H)OC_2H_5 + H_2O \rightarrow$$

$$CH_3C(OH)(H)OC_2H_5 + HCl \rightarrow CH_3COOH + C_2H_5OH + HCl.$$

Although, then, Kastle and Frazer had, in 1898, advanced *the vital points* of Stieglitz's paper, Stieglitz did not acknowledge their priority in the matter.

(2) Mr. Stieglitz's "*our* point that the acceleration.....is due to salt and ion formation" was proposed by Euler[1] in 1901, three years before Mr. Stieglitz's paper appeared. But Mr. Stieglitz did not refer to Euler, who said: "All of these catalytic phenomena....depend upon the increase or decrease of one or more of the substances entering into the (noncatalyzed) reaction; or, by applying electro-chemical principles to all chemistry, they depend upon the increase of the reacting ions." Mellor, in his "Statics and Dynamics," says: "Euler defines a catalytic agent as *a substance which modifies the velocity of chemical reactions by changing the concentration of the ions of the reacting substances.*"

Further, Euler has recentlysaid[2] "I believe that I have found new proof for my former ideas on catalytic reactions. The compound formed by the ester, or cane sugar, and the mineral acid, which is really the reacting (active) molecule or ion undergoing hydrolysis, has been detected or measured in the catalytic hydrolysis of glycine anhydride. On the other hand, experiments have shown that racemic tartaric acid esters are saponified asymmetrically by optically active acids, a result that can hardly be interpreted otherwise than by the assumption that the compounds formed by the union of the optically active catalyzers, acids, with the two optical opposites, esters, differ in concentration and reactivity."

(3) The writer had been engaged in research work two years before going to Chicago. He began the independent study of catalysis in 1899 by collaborating with Hinkins on the reversible formation and hydrolysis of esters by enzymes and bacteria, and by investigating the formation and reactions of urazole esters. Our idea that *catalyzers accelerate such reactions through double-compound or salt formation* was expressed[3] by the sentence (p. 372): "Hence we are very

[1] See Z. physik. Chem., **36**, 644.

[2] Z. physiol. Chem., **83**, 146. See also pp. 147–152.

[3] Acree and Hinkins: THIS JOURNAL, **28**, 370. A number of papers have appeared in various dental journals.

sure that if any changes take place according to the above equation, *the enzyme must take part in the reaction or act as a catalytic agent,*" and by the definite use (p. 372) of *enz.* $C_6H_{11}O_5Ac$ (enzyme-ester salt!) and *enz.* $C_6H_{11}O_5OH$ (enzyme-glucose salt!) in our equations. Following this idea, we showed that such ester salts (see equation, page 372) can be formed and also hydrolyzed, and consequently that the assumption of such salts leads to the experimental facts in reversible reactions. We showed further that the equilibrium point produced by enzymes is different from the *natural one* produced by acids, as has been again demonstrated by Bodenstein and Dietz;[1] that the velocity of the hydrolysis of esters by enzymes is different from the *natural one* produced by acids, as has been also shown by Bodenstein and Dietz; and that the velocity of the hydrolysis of esters by enzymes is proportional to the concentration of the enzyme, just as in the catalysis by acids (p. 376). All of these facts were in harmony with our idea that the basic and acid groups of the enzymes cause salt formation and decomposition. Stieglitz was aware of our independent ideas and of our results, worked out in the Columbus Memorial Laboratory in Chicago and published two years before his article, but he failed to credit us with priority in these ideas.

(4) It seems to me that Mr. Stieglitz deserves credit, not for the idea (Kastle's) of salt formation and its consequences, but for showing clearly for the first time (p. 745) "that the simple application of our common laws of equilibrium to the proved fundamental idea (Kastle's)[2] of salt formation led, mathematically and chemically, directly to the three" so-called laws of catalysis. But even Mr. Stieglitz's keynote or "point that the acceleration . . . . is, as a matter of experiment, due to salt and ion formation" had already been proved quantitatively in a similar case of catalysis by Bredig and Walton,[3] and published in January, 1903, or about eighteen months

[1] Z. Elek. Chem., **12**, 605. Dietz: Dissertation, Leipzig.

[2] My words.

[3] Z. Elek. Chem., **9**, 118. See also *Ibid.*, **10**, 586; **11**, 528. Z. physik. Chem., **47**, 185.

before Stieglitz's paper appeared, and these chemists pointed out the bearing of their work on the hydrolysis of esters and cane sugar. Stieglitz, however, did not mention Bredig and Walton, or their priority in the proof of this fundamental point.

These chemists proved quantitatively that *iodide ions accelerate the velocity of the decomposition of hydrogen peroxide because an intermediate iodoso ion is formed*, as demanded by the mass law,

$$H_2O_2 + \overline{I} \rightarrow H_2O + \overline{IO},$$

(measurably slow reaction)

or

$$\frac{dC_{IO}}{dt} = KC_IC_{H_2O_2},$$

and is decomposed by hydrogen peroxide as follows:

$$H_2O_2 + \overline{IO} = H_2O + O_2 + \overline{I}.$$

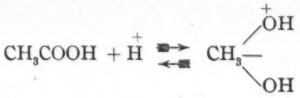
(immeasurably fast reaction)

After this quantitative use of the mass law in catalysis in the proof (to which Mr. Stieglitz does not refer) of the "point that the acceleration . . . . .is, as a matter of experiment, due to salt and ion formation," Bredig and Walton made the following suggestions with reference to the catalysis of esters and cane sugar (p. 118, footnote): "The similarity of the catalysis of hydrogen peroxide by iodide ions to the inversion of sugar and the hydrolysis of esters by hydrogen ions leads to the idea that these catalytic reactions are also to be considered as consecutive reactions involving the addition and loss of the catalyzer (that is, the formation of hydrogen ion hydrates, according to Noyes, or of compounds from the cane sugar, or ester, and the acid, according to Baeyer and others)."

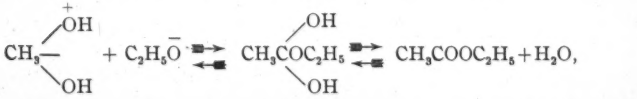
Bredig's quantitative work on the catalysis of hydrogen peroxide by iodide ions is as good evidence of the correctness of the views of Kastle, Euler, Acree, Bredig, Lapworth, Stieglitz, and Goldschmidt on the hydrolysis of esters, as was Mr. Stieglitz's work on imidoesters.

(5) Mr. Stieglitz's "point that the acceleration....is, as a matter of experiment, due to salt and ion formation" was also proposed by Lapworth and described in Mellor's "Statics and Dynamics" in 1904, although Stieglitz did not, in a public address on April 6, 1907, and in his recent note, give Lapworth credit for these ideas.

Mellor says (p. 289): "None of these expressions take account of the accelerating influence of hydrogen ions, and A. Lapworth, in consequence, has proposed a compromise between the ionic theory and the association hypothesis, namely, that 'the production of complex ions is at the bottom of a large number of organic reactions.' He suggests for the esterification of alcohol....



a slow reaction, followed by the more rapid changes—



which are in harmony with the observation that the velocity of hydrolysis of ethyl acetate is directly proportional to the concentration of the hydrogen ions."

(6) In 1906, and again in 1907, Heinrich Goldschmidt[1] proposed the idea that "it seemed possible to decide, by suitable combinations of catalyzing acid and the acid to be esterified, whether the intermediate reactions, which we are led to assume by the present views of catalysis, take place between the alcohol and the catalyzer or between the catalyzer and the acid which is to be esterified." But in at least one public address and in the note just published Mr. Stieglitz has overlooked Goldschmidt's ideas, which are practically the same as his own.

(7) We see then that Kastle, Euler, Acree, and Bredig all had priority over Mr. Stieglitz in every one of his funda-

[1] Goldschmidt and Sunde: Ber. d. Chem. Ges., **39**, 711. Goldschmidt and Udby: Z. physik. Chem., **60**, 728.

mental ideas. Mr. Stieglitz put forward our ideas again as his own, without mentioning the name of any one of these four chemists, who had all "departed from the old idea" and "left the old beaten track." Mr. Stieglitz was informed several months ago by me that they have priority in these ideas, and that Acree and Johnson would give credit where it is deserved. Acree and Johnson gave full credit[1] in their article to all of the above colleagues, and to Stieglitz, in many places, and criticized some of the articles in the light of the most recent knowledge.

Mr. Stieglitz will get credit for his work on imidoester hydrolysis when he publishes it and shows us that he has proved that imidoester cations are hydrolyzed. His quantitative work will be a welcome and, I am sure, valuable addition to that of his colleagues.

(B) And now we come to the work in which Acree and Johnson claim priority over every one except Abel[2] and Euler,[3] whose work was published in German and reached America after the article by Acree and Johnson was in the hands of the editor. I did not claim priority,[4] as Stieglitz would have his readers believe, for *Kastle's idea of intermediate salt formation*, but I do share in the idea, and do claim priority, with Abel and Euler, for the view that the second and third laws of catalysis do not hold in some reactions. It was after very thoughtful consideration of the subject that we chose our experimental material and disproved the validity of the above two laws of catalysis.

Mr. Stieglitz not only presented as new the ideas already advanced by others, but, I take it from the *indirect* statement "there is not one single new principle presented in Acree's paper," that Mr. Stieglitz would now have his readers believe that *he* deserves credit for the discovery by Acree and Johnson that the second and third laws of catalysis do not hold

[1] *Loc. cit.*, pp. 299, 300, 301, 335, 338, 339, 342, 345.
[2] Z. Elek. Chem., **13**, 555.
[3] Z. physiol. Chem., **52**, 146.
[4] See Acree and Johnson: THIS JOURNAL, **38**, 299, 300, 301, 335, 337, 338, 339, 341, 342.

in all reactions. Mr. Stieglitz does not face the issue squarely and state that he presented in the St. Louis report any ideas or experimental material that proved that the second and third laws do not hold in some reactions; his own words would be against him. I believe that if Mr. Stieglitz had at that time really had the very important idea that the second and third laws do not always hold, he would have been as eager then as he is now to get credit for the fact and would have said something about it in his St. Louis address. I quote Mr. Stieglitz concerning this second "so-called" law of catalysis, which postulates direct proportionality between the concentration of the catalyzer and the reaction velocity.

Mr. Stieglitz states, in discussing the catalysis of esters, that (p. 745) "the simple application of our common laws of equilibrium to the proved fundamental idea of salt formation led, mathematically and chemically, *directly to the three principles mentioned above.*" [1] Again, on p. 282 of the St. Louis paper: "We find that the velocity must in fact increase directly proportionate to the concentration of the hydrogen ions.....This consequence of our theory is evidently in perefect agreement with the well-known experimental results." On p. 283: "We find again that the change in the velocity of esterification demanded by the application of this theory is simply proportionate to the change in concentration of the hydrogen ions—which agrees with experience." Again, on p. 283: "The three important characteristic features of the catalysis—a velocity proportionate to the concentration of the hydrogen ions....all are in perfect agreement with this simple conception of the manner in which the catalyzer produces its apparently marvelous result."

Mr. Stieglitz did not intimate in *one* place in his article that he had any experimental material or ideas that would lead him to suspect that the second law of catalysis does not hold in all reactions. Acree and Johnson predicted theoretically and proved experimentally that the *second law of catalysis cannot hold in such cases as* (p. 349) *the hydrolysis*

[1] Italics are mine.

of oximes and (p. 352) *the rearrangement of acylhalogenaminobenzene derivatives and other similar reactions.*

I quote Mr. Stieglitz's only words concerning the third "so-called" law of catalysis, which postulates that a change in the concentration of a catalyzer will not affect the equilibrium point of reversible reactions. Mr. Stieglitz says (p. 283, St. Louis report): "In other words the addition of the catalyzing acid will not affect the ultimate condition of equilibrium between ester, water, acid, and alcohol." Again, on p. 284: "the catalyzer apparently acting only by its presence and not changing the final condition of equilibrium."

I do not find anywhere in Mr. Stieglitz's article an intimation that he had any experimental material or ideas which would lead him to suspect that the third law of catalysis does not hold in all reactions. Acree and Johnson predicted theoretically and proved experimentally that the third law of catalysis cannot hold in such cases as (pp. 349, 351) with the oximes and, *in general*, (p. 351, 353) "in those reversible reactions in which the velocity of one reaction is accelerated in proportion to the m power of the concentration of the catalyzer while the velocity of the reverse reaction is accelerated in proportion to the n power of the concentration of the catalyzer."

I both told and wrote Mr. Stieglitz *in detail*, in a friendly way, in *April and May*, that our theoretical and experimental conclusions disproved the validity of the second and third laws of catalysis, and he will doubtless give us credit for this in THIS JOURNAL, in his forthcoming article, which was received by the editor on Sept. 13. After he knew my results he tried, in a letter to me, to make it appear that he had predicted the same in his St. Louis paper; I have quoted his real conclusions above. It should be pointed out that Abel, Euler, and Miller and Clark[1] have all recently come to our conclusions theoretically and experimentally.

Acree and Johnson, and Acree and Nirdlinger[2] discussed a number of reactions which are catalyzed in a positive or nega-

[1] J. Physic. Chem., **11**, 353.
[2] THIS JOURNAL, **38**, 489.

tive sense by *bases*, *acids*, and *salts*, and showed in which the *active molecules* are *anions*, *cations*, or *neutral molecules*. We greatly broadened, both mathematically and experimentally, the point of view presented before by Kastle, Euler, Acree, Bredig, Lapworth, *Stieglitz*, Goldschmidt, and others, giving in every case full credit to each worker.

(C) The impression that might be left with the reader by Mr. Stieglitz's section (2) (p. 745) that I spent the summer of 1905 in Chicago "to get Stieglitz's methods" and "discussing freely and with my consent with my collaborators, whose work was already completed, the ideas and investigations carried on in our laboratory," is not in accordance with the facts. I worked on *tautomeric compounds*, and was then directing graduate students in Johns Hopkins University in this line of work. While there I invited Mr. Stieglitz to collaborate with me (on tautomerism, and *not* on catalysis) for our mutual benefit, as he had published a paper[1] on tautomeric compounds in which some wrong[2] ideas were advanced. We did not work together, nor did we converse one hour during the summer. *Absolutely* the only thing that I knew of Mr. Stieglitz's work was learned in perhaps a ten-minute talk with one of my former students (Schlesinger), who told me that he had shown that imidoester cations are hydrolyzed; for this fact Mr. Stieglitz was given ample credit[3] by Johnson and myself. I refreshed Mr. Stieglitz's memory on these matters in September, 1907, orally and later by letter.

On April 1, 1907, a week before Mr. Stieglitz's address at the Johns Hopkins University, an article by Acree and Johnson[4] appeared, in which they showed that the second and third laws of catalysis cannot hold in all reactions. Mr. Stieglitz was made aware of these results before his address.

In answer to Mr. Stieglitz's statement (note, p. 745) that the salts of esters and acids were treated by him "as oxonium bases, exactly as Acree has also now done," I must answer

[1] J. Am. Chem. Soc., **25**, 1119.
[2] Acree: This Journal, **37**, 72.
[3] Acree and Johnson: This Journal, **38**, 299, 301, 335, 338, 339, 342.
[4] *Ibid.*, **37**, 410.

(1) that Mr. Stieglitz failed to mention in his St. Louis paper that Kastle,[1] Collie and Tickle, Baeyer and Villiger, Werner, Brühl, Archibald and McIntosh, Walden, van't Hoff, and a host of others had treated them as oxonium bases and salts long before, and (2) that Acree and Johnson, on p. 337, gave *four different structures* for these salts and said: "All four may be in tautomeric equilibrium."

JOHNS HOPKINS UNIVERSITY,
Dec. 13, 1907.

REVIEW.

GLEICHGEWICHTE DER STEREOMEREN. Von W. MEYERHOFFER, Weil. Prof. Dr. Mit einem Begleitwort von PROF. DR. J. H. VAN'T HOFF, und 28 Figuren im Text. Leipzig und Berlin: Druck und Verlag von B. G. Teubner. 1906. pp. 71.

A feeling of sadness comes over one on reading this little monograph. It is the last contribution to physical chemistry from that earnest and fruitful investigator, Meyerhoffer. Cut down at the height of his activity, he will ever be remembered by his colleagues and friends as a distinct loss to our science.

A paragraph from the preface by van't Hoff will show the attitude of this great leader towards his younger colleague.

"Die 1892 gleichzeitig deutsch und französisch erschienene Stereochemie war seine erste grössere zusammenfassende Arbeit; die jetzt 14 Jahre später, erschienene Veröffentlichung auf demselben Gebiet sollte die letzte sein. Sie berührt dasjenige in der Stereochemie, was allgemein auch den Nichtchemiker interessiert, nämlich die Frage, ob die optische Aktivität eine Lebensaüsserung ist, auf welchen Standpunkt sich bekanntlich Pasteur stellte. Die Entdeckung, dass die Trennung der entgegengesetzt aktiven Isomeren und damit die Ausscheidung derselben eine Temperaturfrage ist und mit einer bei bestimmter Temperatur eintretenden Umwandlungserscheinung zusammenhängt, brachte die Erscheinung in anderes Licht, und die vorliegende Arbeit gibt die Gesetze, welche diese Umwandlungserscheinung beherrschen. Dieselben bringen die Ausscheidung von optisch-aktiven Verbindungen in nahen Zusammenhang mit der Spaltung von Doppelsalzen."

The aim and result of the work recorded in this monograph is summarized in the above paragraph. H. C. J.

[1] For references see Acree and Johnson: *Loc. cit.*, p. 298.